THE JOURNAL

OF THE

American Medical Association

Published Under the Auspices of the Board of Trustees

VOL. 167, NO. 9 — CHICAGO, ILLINOIS — JUNE 28, 1958

COPYRIGHT, 1958, BY AMERICAN MEDICAL ASSOCIATION

.958
167

PHYSICIANS TO THE WORLD

PRESIDENT'S ADDRESS

Gunnar Gundersen, M.D., La Crosse, Wis.

IN ACCEPTING the office of President of the American Medical Association, I do so with deep feelings of appreciation, humility, and responsibility. My sense of responsibility is heightened by realization of the tremendous number and variety of challenges which medicine faces today. As individual physicians, members of organized medicine and citizens in the community and the nation, we have in recent decades encountered an ever-increasing complexity of demands on our time and thought. Now, like all of our fellow Americans, we find our problems compounded by the world struggle for survival and freedom—in the new age of hydrogen bombs, ballistic missiles, and earth satellites.

In recent years the individual physician has had an increasingly difficult time in trying to keep up with the accelerated scientific advances in medicine. Now, with man probing into outer space, it appears that our scientific future will be further complicated by the development of still another specialty—space medicine. Nevertheless, right here on terra firma it is more than ever true that medicine is a lifelong study—one which actually is just beginning when the young doctor receives his M.D. degree or completes his graduate training.

Meanwhile, we also are reemphasizing the emotional, personal, and spiritual factors in medical care. The age-old art of medicine—that intangible element made up of compassion and warmth—is regaining its proper place. In medicine, as in all other phases of American life, we are rediscovering that philosophy is just as important as technology, that the human personality cannot be subordinated to crisp efficiency.

The challenge of how to apply the science and art of medicine is formidable enough in itself. But it too has been further complicated by the changing backdrop on the American scene. Over the past 20 years we also have been called upon to consider a snowballing trend of social, economic, and political developments affecting medicine.

These problems are related to still another area—one in which we have obligations and responsibilities shared by all our fellow Americans. This is the broad arena of citizenship. We as individuals have the duty to bring our weight to bear on the vital question of whether the individual or the state shall stand supreme in America's future.

Obligations of the Physician

Certainly, one might say, all of that should be more than enough to ask of a physician or his profession—scientific excellence, concern for the patient as a human being, active effort to solve medicine's socioeconomic problems, and full discharge of the responsibilities of citizenship. I would, however, call your attention to still another challenge, still

Read before the 107th Annual Meeting of the American Medical Association, San Francisco, June 24, 1958.

another set of demands. In this day and age—a time of terrible decision—we also must consider our obligations to all of humanity. As both physicians and citizens we must see that medicine plays its full role, not only in promoting better world health but also in helping the search for brotherhood and peace.

Some of you may be saying to yourselves, "With all our local, state, and national problems, how can we possibly find time to do anything about world health? What is the connection?" That, of course, is a natural reaction in view of the growing complexity of our professional life.

I would answer in two ways—one dealing with tradition and one with the realities of the present. The traditions of modern medicine began many centuries ago with Hippocrates, the Greek physician and teacher. Students from all over the Aegean area gathered around him on the island of Cos. From there they returned home to spread the knowledge and ethics which Hippocrates had taught them. And it is important to remember that when Hippocrates wrote the medical oath which all of us have taken he was speaking not just to and for Greeks; his words speak a universal language that applies to all men. So, ever since those distant days on the island of Cos, dedicated physicians have made their knowledge and compassion available to all who needed them.

Turning to present-day realities, I am convinced by personal experience that our medical heritage—which stems from Hippocrates—can be applied more widely, more effectively, in today's troubled world. As many of you know, I have been active for several years in the affairs of the World Medical Association. As a delegate in its General Assembly and a member of its Council, I have had the opportunity to meet hundreds of physicians from more than 50 countries. And I have learned that they sincerely desire closer understanding and cooperation—not only on scientific and professional matters but also on a human basis. There is growing recognition that medicine, with its resources and influence fully mobilized, can perhaps do more for world peace than the billions of dollars being poured into armaments. There is mounting conviction that the time has come when medical statesmanship must be used to augment the methods of political diplomacy.

I firmly believe that we can and must expand our vision and face up to this new challenge. The problems which trouble us here at home exist also for the physicians and peoples of other lands. The knowledge, ideas, and experience which we have gained can help them. But we also can benefit from learning more about their difficulties—how they might have avoided some, how they are trying to solve others. Our international obligations are simply extensions of our local responsibilities.

The common thread is a concern for human life and health, a respect for personal freedom and dignity. In my opinion, there is a clear, logical, mutuality of interest.

If we think we have difficulty in keeping up with medical advances, let us consider the thousands of physicians, nurses, and technicians throughout the world who carry on their work with only a fraction of the facilities, equipment, journals, books, exhibits, and other aids which are available to us. For many of them, just this one-week meeting in San Francisco would be the professional event of a lifetime.

If we think that our patients should have more sympathy and understanding, we who are bestowed with the blessings of our country must consider the millions of persons in other parts of the world who are diseased, undernourished, crippled, or dying. To them, just one kind look, one gentle word, one soothing drug would be like a miracle.

If we think that we have socioeconomic problems in American medicine, let us consider the plight of physicians and patients in those countries where there are extreme shortages of doctors, where people still pay medicine men and witch doctors for their incantations, or where medical care long has been used as a political football. In the latter case, let us learn well the lesson of medical unity.

If we think that our freedoms are threatened here at home, let us consider the millions who already have been subjugated by authoritarian philosophies or who are being victimized by constant, ruthless pressure and exploitation in the cold war between communism and democracy—a war that really can be won only by ideas, not by missiles or bombs.

As physicians, our first obligation is, of course, to our patients. But as members of the medical profession, our obligation extends to all mankind.

The Physician and World Peace

As American citizens our first duty is to this country. But as members of a civilization which believes in the brotherhood of man, we also have a duty toward all men who yearn for freedom, dignity, peace, and health. Physicians in America should never forget their responsibilities to all humanity or neglect their opportunities to promote the brotherhood of man.

We physicians have a unique opportunity to provide a spark of leadership which can help bring the world closer to the dream of world brotherhood. If you do not feel the compulsion of that task, I can only remind you of the Sputniks, Explorers, and Vanguards whirling overhead. They in themselves are but the toys of grown men, compared with the potential engines of destruction which put them into orbit. If our alternative is destruction or a dream, the only sensible choice is to make the dream work.

Medicine can play a vitally effective part in bringing reality to the dream of world peace. For medicine, despite the designs of politicians or dictators, is above the harsh conflicts of ideologies and power politics. Medicine, like religion, speaks a universal language which passes all barriers of race, creed, color, and nationality. Already, great work has been accomplished by individuals, private organizations, medical associations, and official agencies. In fact, the brightest chapter in the international story since World War II is that on health and medicine. This is no uncharted course; the way is well marked.

San Francisco is a particularly appropriate place in which to stress the challenge of international cooperation. For it was here in 1945 that the United Nations was formed and the first suggestion was made for establishment of a new international health organization. Three years later the World Health Organization came into being.

While the World Health Organization was going through its formative stages, the physicians of many countries were meeting informally to discuss the need for an international medical organization. As a result, the World Medical Association was officially established in September, 1947, with the American Medical Association as a founding member.

Thus, both organizations—rooted in postwar ideals of world collaboration—have just recently completed their first decade of service. From the beginning, they have maintained close liaison with one another and with many additional international groups interested in various phases of medicine, health, and general welfare. They are the main avenues for mobilizing and coordinating world medical resources for the common good of humanity.

Whereas the World Health Organization represents governments and the field of public health, the World Medical Association speaks for the medical profession. It now is composed of 53 national medical associations representing about half a million physicians throughout the world. Its principal objectives are to maintain the standards, ethics, and traditions of medical practice; to raise the standards of medical education; to promote the mutual exchange of information and ideas among the physicians of the world; to help raise the level of world health; and to promote world peace.

In pursuit of those objectives, the World Medical Association has carried out a wide variety of activities. As just one example, in 1953 the World Medical Association sponsored the First World Conference on Medical Education. More than 600 participants from over 60 countries and 127 universities and medical schools attended that London meeting, which focused attention on undergraduate medical education. The proceedings have been widely distributed throughout the world. The Second World Conference on Medical Education—spotlighting the theme of "Medicine as a Lifelong Study"—will be held next year in Chicago, where we of the American Medical Association will be hosts to our medical colleagues from other lands.

Another new avenue of approach to help the cause of international peace is the Medicine and Health Professions Committee of the People-to-People Program, initiated last year by President Eisenhower. This program is designed to promote close contacts and friendships among individuals and groups who share professional, cultural, and economic interests. It is based on the idea that if the people of the world could begin to know one another—to meet, talk, correspond, and exchange visits—many of the world's troubles would be over. We might then begin to use the knowledge of the atomic age for humanity, rather than in an attempt to destroy our civilization.

American doctors, medical missionaries, nurses, and technicians—serving humanity in far flung parts of the world—are contributing immeasurably to this great cause. The work of some of them was beautifully reported last January in the March of Medicine telecast called "M.D. International." They were described as unofficial American ambassadors of good will—men and women who are demonstrating the forceful good that lies in the basic brotherhood of man, who are revealing our greatest hope for the future—man's humanity to man.

President Eisenhower recently pointed out that the armed forces of the United States are only supports for the much larger purpose of a just peace and the advancement of human well-being at home and throughout the world. In the struggle for peace, he said, "the strength that endures rests with those who live in freedom." And he added that "tyranny is too brittle—too insecurely based—too dependent upon force and brutality—too contrary to the hopes and ideals of humanity—to last over the long pull."

Physicians, alerted here and abroad, can do much to advance the cause of freedom and human well-being. For medicine, by its very nature, speaks a universal language dedicated to scientific truth, humanitarian service, individual dignity, and world peace. In medical science there are no secrets, no iron curtains, no cold war. To physicians everywhere, atomic energy means a new way of fighting disease, not a new way of conquering the world. Medicine exists to save life, not destroy it.

The demands of these troubled times require that we perform at only one level—our very best. The time has come for medical statesmanship which will help point the way toward better health—and a better life—for all the peoples of the world.

TREATMENT OF THE DUMPING SYNDROME

George L. Jordan Jr., M.D., Houston, Texas

It is important to recognize that the actual incidence of the dumping syndrome is high in the untreated patient, for by proper dietary management in the early postgastrectomy period these symptoms can be prevented, so only a small percentage of patients need ever have any significant difficulty. The ideal treatment for this syndrome would be prevention, and various techniques of gastrectomy have been advocated by different authors to produce a low incidence, but no technique has been uniformly successful in the hands of all investigators. Approximately one-half of the patients with mild symptoms desired no treatment at all, and most of the remainder were satisfactorily managed by diet or postprandial recumbency. None of the patients classified as having severe symptoms could be managed by diet or by the combination of diet and recumbency; however, the condition of several of these patients was improved by the use of antispasmodics and by blood transfusions.

The dumping syndrome is a complex physiological response to the presence of undigested food in the jejunum. The ideal therapeutic approach must await further investigation, for all of the factors involved in the pathogenesis of this syndrome have not been clearly defined. Nevertheless, therapeutic regimens based upon an understanding of pathophysiological alterations now delineated may relieve symptoms.

Diet

There is general consensus that dietary management is the basic factor in treatment.[1] Proteins are tolerated better than carbohydrates and solid foods better than liquids, for carbohydrates are hydrolyzed into osmotically active substances more rapidly than are proteins, and foods in the liquid state enter the jejunum rapidly. Studies of the effect of fat in the diet have not given consistent results, but there is some evidence to indicate that the form in which fat is administered may influence the production of symptoms. Thus, homogenized fats, particularly those fat solutions containing carbohyrates, are more likely to produce symptoms than are those fats of large molecular weight in the naturally occurring state.[2] Emptying of the gastric remnant is not dependent upon gastric peristalsis.[3] Therefore, administration of fat does not improve symptoms by slowing passage of food into the jejunum.

With these facts in mind, one should take a careful dietary history. Symptoms may occur after the ingestion of specific foods; such foods should be eliminated from the diet. For patients with symptoms more difficult to control, a strict dietary regimen should be outlined, consisting of six small daily feedings, high in protein, low in carbohydrate, and containing a moderate amount of fat. Milk is poorly tolerated by many postgastrectomy patients; consequently, it should be eliminated from the diet, as should ice cream, milk shakes, pies, and other sweets. Each meal should be eaten dry, and fluids taken between meals should contain a minimal amount of sugar or none at all. A dietary regimen of this type may give satisfactory relief in many patients. Robinson and Pittman [1c] found that complete or partial relief was obtained in 80% of patients studied.

Postprandial Recumbency

Those patients who need additional help may lie down for 20 to 30 minutes in the immediate postprandial period. Amdrup [4] found that the injection of stimulating foods directly into the jejunum caused symptoms, regardless of posture, but when foods were taken orally symptoms were less if the patients was recumbent. Roentgenographic studies demonstrate that gastric emptying is slower when the patient is in a recumbent position, and this appears to be the primary effect of this maneuver.[3] Unfortunately, many patients do not always have access to a bed after meals.

Antispasmodics

The most extensive study of the use of antispasmodics was reported by Rauch and Bieter,[5] who investigated a number of drugs and found that atropine was rarely beneficial, whereas methantheline (Banthine) bromide relieved 26% of the group. An experimental drug produced complete relief in 35% of the patients treated, but unfortunately it resulted in so many undesirable side-effects that clinical use on a large scale was not practical. These authors found that β-diethylaminoethyl 9-fluorenecarboxylate hydrochloride (Pavatrine) was the most effective drug, free of side-reactions, giving complete relief in 22% and partial relief in 30% of the patients. Capper and Welbourn [6] state that drugs have proved disappointing. These authors used hexamethonium bromide, hoping to block the autonomic ganglions and reduce visceral sensation. Studies in this clinic indicate that the effect of antispasmodics is primarily that of decreasing jejunal motility, thereby decreasing the speed of gastric emptying as well as decreasing nausea, vomiting, and diarrhea.[2a] Since most of the antispasmodics have an anticholinergic action, they may also be of value in decreasing the

From the Cora & Webb Mading Department of Surgery, Baylor University College of Medicine, and the Department of Surgery, Veterans Administration Hospital.

passage of fluid into the gastrointestinal tract, though this latter action has not been demonstrated objectively.

When utilizing antispasmodic drugs, it is important to realize that the response in the fasting state is quite different from the response in the postprandial state and that the response of a given individual to various antispasmodics differs. By trial and error one may establish the drug which produces the maximum effect. In clinical practice, it is desirable to start therapy with a drug which has minimal side-effects, for dryness of the mouth, blurring of vision, or urinary retention may be as distressing to the patient as his dumping symptoms. A drug may be administered empirically for a period of one to two weeks and the effect assessed. If the patient obtains a good result, it is quite likely that this effect will be persistent. If the first drug tried does not produce symptomatic relief, additional drugs should be employed until the proper one is found, for failure to respond to one drug does not preclude an excellent response to another. An occasional patient will have complete control with administration of the drug alone; however, dietary measures will also be required in most patients. Failure to obtain control of symptoms with a combination of diet, antispasmodics, and postprandial recumbency is rare except in patients with very severe symptoms.

958
167

Blood Volume Replacement

Since the work of Roberts and her associates,[7] other investigators [8] have confirmed the finding of a decrease in blood volume in the immediate postprandial period, which coincides well with the symptomatic period. Many observers feel that this alteration is of significance in production of vasomotor symptoms, though it is probably not as important as first believed.

Most patients with this syndrome have a normal blood volume; however, a few patients have a depleted blood volume resulting from inadequate nutrition, and this may impair their ability to withstand these postprandial hemodynamic changes. Therefore, the blood volume should be determined in those patients who fail to respond to the measures already mentioned, for restoration to normal may result in significant symptomatic improvement and convert an intractable condition to one managed satisfactorily by diet or antispasmodics.[9]

Potassium Salts

On the basis of electrocardiographic changes occurring in the postprandial period, Smith [10] suggested that acute alterations in serum potassium concentration might play a role in symptom production, and Kleiman and Grant [11] reported good results with the use of potassium salts clinically. There is some evidence to indicate an inverse relationship between the magnitude of fall in the serum potassium concentration and the fall in blood volume during the symptomatic period.[8] Therefore, the role of potassium changes in the production of symptoms is not completely settled, but in the minds of most investigators alterations in serum potassium concentrations are of little or no significance. From a clinical standpoint, the good results reported by Kleiman and Grant have not been duplicated by others.[6]

Psychotherapy

There are those who maintain that this syndrome is primarily functional in origin and that many patients may be successfully treated by psychotherapy.[12] Some postgastrectomy patients have psychoneurotic symptoms which may be confused with the dumping syndrome; and some patients who have the dumping syndrome will, in addition, have psychoneurotic tendencies which make management of their problem more difficult. Certainly many of these patients will be improved by psychotherapy, and in most instances the physician in charge of the patient will be able to accomplish this. In addition, reassurance that the symptoms do not signify a serious disorder will relieve anxiety in many patients. Nevertheless, the weight of evidence which has been accumulated in the past years leaves little doubt that the dumping syndrome, as described herein, is the result of physiological abnormalities, and, therefore, psychotherapy should be used as a therapeutic adjunct rather than the primary approach to treatment.[13]

Leonard and his associates [14] have recently reported the use of hypnosis to control severe symptoms in some patients. We have had no experience with this procedure, but its use may be justified in those patients with intractable symptoms.

Other Nonoperative Measures

Welbourn states that Kay regards the administration of an oral local anesthetic, such as procaine hydrochloride, a valuable therapeutic measure, but he was unable to verify these observations.[6] Glazebrook and Wrigley state that symptoms have been relieved in some patients by the administration of sodium bicarbonate, and Capper and Welbourn [6] have noted similar results. We have administered this drug occasionally without success. Butler treated 61 patients by paravertebral injection of procaine hydrochloride and obtained relief in 50 of these. Improvement in symptoms was transitory in most, but in four the effect appeared permanent, as no symptoms had returned after several months.[15]

Surgery

Each of the measures noted above should be attempted before surgical intervention is considered, but the few patients who fail to respond may obtain some relief through operative modification of their gastrointestinal anastomosis. This subject has been extensively reviewed by Capper and Welbourn,[6] who collected 14 patients treated by support of the lesser curvature and afferent loop, with 79% relief; 9 patients with jejunal replacement had 100% relief; 30 patients with colonic replace-

ment had 80% relief; and 63 having conversion to Billroth 1 anastomosis had 84% relief. Unfortunately the follow-up period is short in all of the reported cases; therefore, the high incidence of symptomatic improvement must be accepted with some reservations. All but one of these procedures is basically a conversion to the Billroth [1] anastomosis.

Other procedures which have been advocated include jejunoplasty, narrowing of the gastroenteric stoma, vagotomy, and splanchnicectomy. The evidence to date indicates that the procedure of choice is conversion to a gastroduodenostomy, if gastrojejunostomy was originally performed. There is no good evidence to indicate that surgical modification of a gastroduodenostomy is likely to be beneficial. This study was undertaken to assess the therapeutic results obtained in our clinic.

Materials and Methods

The records of 400 patients treated by subtotal gastrectomy were reviewed. Of this group, there were 300 (75%) with duodenal ulcers, 60 (15%) with gastric ulcers, 14 (3%) with gastrojejunal ulcers, 4 (1%) with gastritis and hemorrhage, and 22 (6%) with carcinoma. Of these patients, 144 (36%) experienced symptoms typical of the dumping syndrome. The symptoms uniformly appeared during the meal or within 10 to 20 minutes after ingestion, and were characterized by nausea, with or without vomiting, and occasionally diarrhea, as well as a vasomotor component of weakness, sweating, pallor, and/or increased pulse rate.

TABLE 1.—*Methods of Treating Patients with Dumping Syndrome*

Treatment	Patients with Mild Symptoms		Patients with Moderate Symptoms	
	No.	%	No.	%
None	34	48	8	12
Diet	27	38	17	27
Postprandial recumbency	6	8	1	2
Antispasmodics	2	3	31	48
(Lost to follow-up)	2	3	7	11
Total	71	100	64	100

Symptoms were classified as mild if they occurred only after a very large meal, were of little concern to the patient, or occurred only after the eating of specific foods which could easily be eliminated from the diet. If symptoms occurred once or twice weekly, despite attempts by the patient to obtain relief, they were deemed moderate. Symptoms were classified as severe when they occurred after almost every meal and were incapacitating to the point of interfering with normal activity. There were 71 patients with mild symptoms, 64 with moderate symptoms, and 9 with severe symptoms. (These represented 18, 16, and 2% of the total group and 50, 44, and 6% of the group with dumping syndrome.)

All of the patients with severe symptoms and approximately one-half of those with moderate symptoms underwent specific diagnostic studies (electrocardiography, studies of blood volume, jejunal motility, serum potassium concentration, and/or efferent loop aspiration) to confirm the diagnosis objectively and to exclude other postgastrectomy syndromes as the cause of symptoms. One-hundred thirty-four patients (93%) were followed for periods of six months to four years after the onset of symptoms.

Treatment and Results

Approximately one-half of the patients with mild symptoms desired no treatment at all, and most of the remainder were satisfactorily managed by diet or postprandial recumbency. Only two required antispasmodics in their therapeutic regimen (table 1.) It was possible to obtain complete relief of symptoms in each of these patients.

Of the patients classified as having moderate symptoms, eight desired no treatment and preferred to eat as they liked and experience symptoms occasionally rather than employ a therapeutic regimen. Only one patient obtained satisfactory control by postprandial recumbency alone, though there were six additional patients who utilized this maneuver in combination with dietary control. Almost one-half of these patients required antispasmodics as an aid in symptom control (table 1). Of the 49 patients who desired treatment and who were followed, complete relief of symptoms was obtained in 37% and partial relief in 55%. Of the four patients (8%) who failed to respond to the various regimens employed, one had complete spontaneous relief after a period of two years, one was not properly treated, and the remaining two patients did not desire further attempts at therapy.

None of the patients classified as having severe symptoms could be managed by diet or by the combination of diet and recumbency. Two patients obtained complete relief of symptoms when antispasmodics were added to the regimen, and one obtained partial relief, so that additional measures were not necessary. The remaining five patients failed to respond. One patient subsequently had spontaneous regression so that no further attempts at therapy were indicated. A jejunal pouch was created in two patients. One had partial relief of symptoms for approximately a year, after which time symptoms recurred as severe as they had been previously, while the other patient experienced no relief at any time. The patient obtaining partial relief of symptoms for a short time following operative intervention was subsequently proved to have a low blood volume, and correction of blood volume to normal allowed satisfactory control with diet alone. At the present time he has been followed for 18 months since correction of his blood volume deficit and has done well. The normal blood volume has been maintained.[9]

Of the remaining two patients, one has a severe psychiatric problem in addition to his dumping syndrome, which makes control virtually impossible, while the second patient feels that an attempt

to stay on a strict regimen interferes with his daily activities more than does his symptomatology. He is an aggressive, active businessman who works long hours daily, despite his dumping symptoms. One patient was not traced.

Orally given anesthetics, sodium bicarbonate, paravertebral block, and orally given potassium salts have each been tried. Our experience with these agents is too limited to warrant definitive evaluation, but no patient obtained relief of symptoms. Of the 92 patients who desired treatment, in the early follow-up period 55 (60%) obtained complete relief of symptoms, 29 (31%) obtained partial relief, and 8 (9%) obtained no relief. There were no patients who subsequently became refractory to treatment after having an early good result, but 17 patients (13%) had spontaneous improvement, so that with the passage of time the number of patients with complete relief of symptoms increased. Thus, at the present time 67% of the treated group have complete relief, while only 6% have failed to improve. These six patients represent only 1.5% of the entire group of 400 postgastrectomy patients. Four of these patients have continued to work despite their symptomatology and have not required hospitalization, while two are totally incapacitated.

Comment

The reported incidence of the dumping syndrome varies from 2 to 45%.[16] In all probability much of the difference in incidence reported depends upon the definition of dumping and the detail with which the history was taken. Thus, those patients who can prevent symptoms simply by eliminating offending foods may be listed as having a food intolerance rather than the dumping syndrome. Some authors have classified patients as having the dumping syndrome only if the symptoms were incapacitating. Furthermore, by taking a careful history one finds many patients who deny symptoms except on detailed questioning.

It is important to recognize that the actual incidence of the syndrome is high in the untreated patient, for by proper dietary management in the early postgastrectomy period these symptoms can be prevented, so only a small percentage of patients need ever have any significant difficulty. Our experience indicates that approximately 15% of patients treated by subtotal gastrectomy may need help in alleviation of symptoms. This can be accomplished with patience, reassurance, and proper selection of a therapeutic regimen. Several weeks may be required to establish satisfactorily the best therapeutic regimen for an individual patient. The response to a specific antispasmodic varies from patient to patient, and it may be necessary to try several before the one producing the optimum results is found.

Fortunately, those antispasmodics with the least number of side-effects are as effective as those producing a greater number of side-effects (table 2). All of our patients who obtained complete relief for as long as two to three weeks with the use of antispasmodics have continued to obtain good relief with the use of such drugs for follow-up periods of as long as three years. Once the use of an antispasmodic is necessary, most patients will require its use indefinitely if symptoms are to be controlled.

The ideal treatment for this syndrome would be prevention, and various techniques of gastrectomy have been advocated by different authors to produce a low incidence, but no technique has been uniformly successful in the hands of all investigators. In our patients the Billroth 1 and Billroth 2 procedures were used, as well as jejunoplasty. The total incidence of postgastrectomy symptoms does not appear to be greatly different when the Billroth 1 and Billroth 2 procedures are compared, but only one of the patients with severe symptoms was treated by the Billroth 1 procedure, and this patient was the one who eventually had spontaneous remission of symptoms.

Thus, our observations tend to support those of Capper and Welbourn,[6] who found that the incidence of severe symptoms was lower following gastroduodenostomy. Unfortunately, this procedure is attended by such a high incidence of marginal ulcer when used in the treatment of duodenal ulcer that it cannot be recommended. However, we consider gastrectomy with gastroduodenostomy the treatment of choice for gastric ulcer, since the incidence of marginal ulceration is low following surgical management of this lesion. It is our belief that patients treated for gastric ulceration are less likely to develop this postgastrectomy syndrome than are patients treated for duodenal ulceration, regardless of the surgical procedure employed. It is noteworthy that no patient treated for gastric ulcer developed severe postgastrectomy symptoms.

TABLE 2.—*Results Obtained with Antispasmodic Drugs in Treatment of Dumping Syndrome*

Drug	Patients, No.	Incidence of Symptoms of Relief, % None	Partial	Complete
β-Diethylaminoethyl 9-fluoroenecarboxylate hydrochloride (Pavatrine)	3	100	0	0
Mixture of Dactil and Piptal, 10:1 (Tridal)	2	50	50	0
Pipenzolate methylbromide (Piptal)	10	40	50	10
Methantheline (Banthine) bromide	8	74	13	13
Hexamethonium bromide	12	42	42	16
Belladonna	14	36	43	21
Piperidolate hydrochloride (Dactil)	20	35	30	35

References

1. (*a*) Hayes, M. A.: Dietary Control of Postgastrectomy "Dumping Syndrome," Surgery **37**:785-793 (May) 1955. (*b*) Medwid, A., and others: Physiologic Alterations Resulting from Carbohydrate, Protein and Fat Meals in Patients Following Gastrectomy: Relationship of These Changes to Dumping Sydrome, Ann. Surg. **144**:953-960 (Dec.) 1956. (*c*) Robinson, F. W., and Pittman, A. C.: Dietary Management of Postgastrectomy Dumping Syndrome, Surg. Gynec. & Obst. **104**:529-534 (May) 1957.

2. (*a*) Jordan, G. L., Jr.; Overton, R. C.; and DeBakey, M. E.: Postgastrectomy Syndrome: Studies on Pathogenesis, Ann. Surg. **145**:471-478 (April) 1957. (*b*) Reference 1*b*.

3. Jordan G. L., Jr.; Barton, H. L.; and Williamson, W. A.: Study of Motility in Gastric Remnant Following Subtotal Gastrectomy, Surg. Gynec. & Obst. **104**:257-262 (March) 1957.

4. Amdrup, E., and Jørgensen, J. B.: Influence of Posture on Dumping Syndrome, Acta chir. scandinav. **112**:307-312 (March 28) 1956.

5. Rauch, R. F., and Bieter, R. N.: Treatment of Postprandial Distress Following Gastric Resection, Gastroenterology **23**:347-355 (March) 1953.

6. Capper, W. M., and Welbourn, R. B.: Early Post-cibal Symptoms Following Gastrectomy: Aetiological Factors, Treatment and Prevention, Brit. J. Surg. **43**:24-35 (July) 1955.

7. Roberts, K. E., and others: Cardiovascular and Blood Volume Alterations Resulting from Intrajejunal Administration of Hypertonic Solutions to Gastrectomized Patients: Relationships of These Changes to Dumping Syndrome, Ann. Surg. **140**:631-640 (Nov.) 1954.

8. Peddie, G. H.; Jordan, G. L., Jr.; and DeBakey, M. E.: Furthur Studies on Pathogenesis of Postgastrectomy Syndrome, Ann. Surg. **146**:892-898 (Dec.) 1957.

9. Jordan, G. L., Jr.; Overstreet, J. W.; and Peddie, G. H.: Use of Blood Transfusions in Treatment of Postgastrectomy Syndrome, Surgery **42**:1055-1059 (Dec.) 1957. Mallet-Guy, P.; Devic, G.; and Ricard, A.: Séquelles générales de la gastrectomie pour ulcere et perturbations du volume sanguin: efficacite du rétablissement de la massa sanguin, Lyon chir. **49**:913-930 (Nov.-Dec.) 1954.

10. Smith, W. H.: Potassium Lack in Post-gastrectomy Dumping Syndrome, Lancet **2**:745-749 (Oct. 27) 1951.

11. Kleiman, A., and Grant, A. R.: Role of Potassium in Pathogenesis and Treatment of Postgastrectomy Dumping Syndrome, in Surgical Forum: Clinical Congress of American College of Surgeons, vol. 4, 1953, pp. 296-301.

12. Bell, H. G.: Psychophysiology of Dumping Syndrome, A. M. A. Arch. Surg. **66**:585-586 (May) 1953.

13. Hinshaw, D. B.; Joergenson, E. J.; Davis, H. A.; and Stafford, C. E.: Peripheral Blood Flow and Blood Volume Studies in Dumping Syndrome, A. M. A. Arch Surg. **74**:686-693 (May) 1957. Footnotes 2*a*, 7, 10, and 11.

14. Leonard, A. S.; Papermaster, A. A.; and Wangensteen, O. H.: Treatment of Postgastrectomy Dumping Syndrome by Hypnotic Suggestion, J. A. M. A. **165**:1957-1959 (Dec. 14) 1957.

15. Butler, T. J., and Capper, W. M.: Experimental Study of 79 Cases Showing Early Post-gastrectomy Syndrome, Brit. M. J. **1**:1177-1181 (May 26) 1951.

16. Footnotes 1*c*, 5, and 6.

METASTATIC TESTICULAR TUMOR TREATED WITH NITROFURAZONE

REPORT OF A CASE

Myron J. Szczukowski, M.D., Alvin L. Daywitt, M.D.
and
Harold Elrick, M.D., Denver

A testicular teratocarcinoma occurring in a 35-year-old man was treated initially by surgery and later by irradiation of the inguinal and abdominal regions. Chest films showed an initial absence of pulmonary metastases, but later films showed the gradual appearance of pulmonary lesions until, six months after operation, 12 or 13 such lesions were visible. Administration of nitrofurazone in doses of 0.5 Gm. twice (later three times) a day by mouth was followed by the complete disappearance of some of these nodules. The onset of a severe peripheral neuritis made it necessary to discontinue this treatment. Symptoms of pulmonary involvement recurred, and the chest films revealed an increase in the size and number of the lesions. The patient died of metastases to lungs, liver, brain, pericardium, and regional lymph nodes. This history closely parallels reports by other authors as to the striking therapeutic effects as well as the painful side-effects of nitrofurazone, and indicates the importance of further trials of this drug and its derivatives.

Nitrofurazone (Furacin) has been used perorally in several cases of human seminoma and embryonal carcinoma.[1] In 1952 Friedgood and associates [2] reported four cases of testicular seminoma treated with nitrofurazone. In all of these, there was marked degeneration of the tumor cells, increased fibrosis, and decreased cellularity of the tumor. In 1955, Wildermuth [1b] reported a case of testicular cancer treated with nitrofurazone. The patient had developed widespread pulmonary metastases after a complete course of postorchiectomy irradiation. Nitrofurazone was administered orally, 1.5 Gm. daily for two weeks and then 2 Gm. daily for two more weeks. The patient developed a severe painful peripheral neuropathy, and nitrofurazone was withdrawn. Three weeks later the neuritis improved slightly, but roentgenographically the improvement of pulmonary lesions was so marked that administration of 1.5 Gm. of nitrofurazone a day was started again and continued for one week, when the neuritic pain again became unbearable. The patient's chest film taken on Jan. 21, 1955, was free of recurrences (though pulmonary scars persisted), and he was able to work a full eight-hour day. The patient died in October, 1955, of cerebral metastases, with a survival period of over two years. Another patient was treated but could not tolerate the drug.

The purpose of this paper is to report an additional case of testicular carcinoma with striking temporary decrease of multiple pulmonary metastases after nitrofurazone therapy.

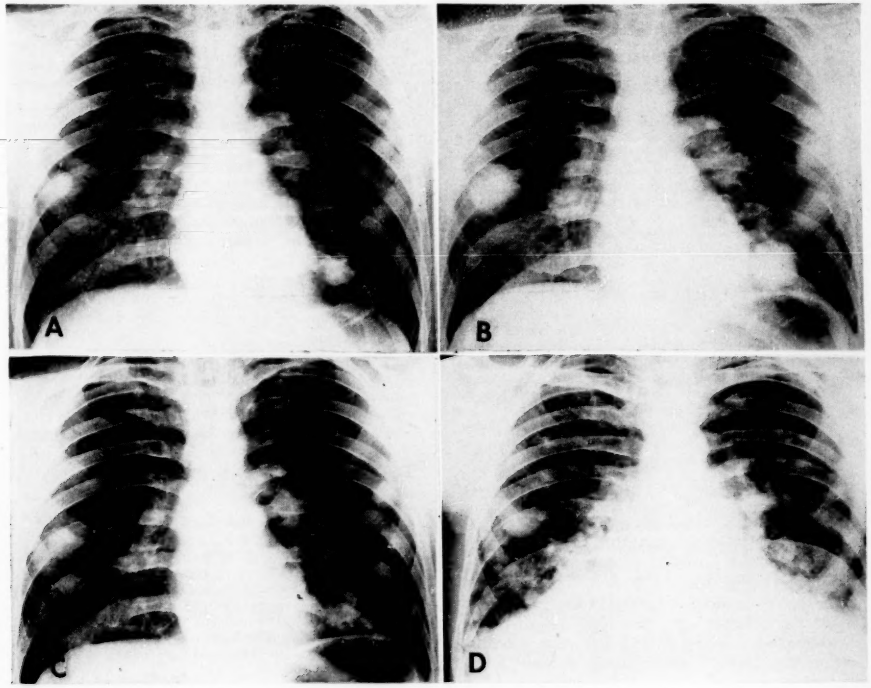
From the radiology and radioisotope services, Veterans Administration Hospital, and the departments of radiology and medicine, University of Colorado School of Medicine.

A 35-year-old man was transferred to the Denver Veterans Administration Hospital on April 18, 1955. He gave a history of having noted an increase in the size and firmness of the right testis for the first time in January, 1955. Some weeks later a small, nodular, tender mass appeared in the right inguinal region. The history was not remarkable except for a right inguinal herniorrhaphy and orchiopexy 18 years previously.

On March 14, 1955, the right testis and right inguinal mass had been removed at the Cheyenne VA Hospital. The histological diagnosis was teratocarcinoma involving the testis and lymph node. Ten days later a radical inguinal femoral and retroperitoneal node dissection was done on the right side. Several of the nodes were found to be involved with metastatic cancer. A chest film revealed no metastases.

Physical examination on admission revealed a well-developed, well-nourished male in no distress. The positive physical findings consisted of a large, infected ulcer of the right groin, tenderness along the course of the saphenous vein, a well-healed surgical scar of the right abdomen, and absent right testis. The heart and lungs revealed no abnormalities and there was no lymph node enlargement. Laboratory tests on admission revealed a normal urine, a hemoglobin level of 15.5 Gm. per 100 cc., and a white blood cell count of 6,300, with a normal differential count. No chest or bone metastases were found at this time.

The patient was given heparin and bishydroxycoumarin (Dicumarol), and the saphenous thrombophlebitis subsided in four days. He was then given abdominal (para-aortic) radiation with 1,000 kv. (3,000 r tumor dose). The right inguinal region was treated with 250 kv. (3,000 r in air). This x-ray therapy was carried out between May 14 and Aug. 1, 1955. On the latter date a chest x-ray showed a small ovoid density in each lung. The frog test for urinary gonadotropins was negative on Aug. 5. The patient was discharged two days later, to be followed as an outpatient by the tumor clinic. A follow-up x-ray on Oct. 4 revealed 12 or 13 soft ovoid densities (0.5 to 3 cm.) scattered throughout both lung fields (see figure, A).



Chest roentgenograms. *A*, Oct. 4, 1955, before nitrofurazone therapy, revealing multiple round metastatic lesions scattered throughout lung fields and hilar areas. *B*, Dec. 12, 1955, showing increase in size of pulmonary lesions. Nitrofurazone therapy was started Dec. 1. *C*, Feb. 24, 1956, revealing maximum regression of metastases. Several lesions disappeared completely. Nitrofurazone therapy (35 Gm.) was completed Jan. 15. *D*, Aug. 28, 1956, showing innumerable metastatic nodules of various sizes scattered throughout lungs. Note that original lesions never increased to pretreatment size.

The patient was readmitted on Nov. 28, 1955, for treatment with nitrofurazone, which was administered perorally in a dose of 0.5 Gm. twice a day from Dec. 1 to Dec. 12 (12 Gm. total). A chest film on Dec. 12 showed an increase in the size of the pulmonary lesions (see figure, *B*). The next day a small intestine obstruction developed and was relieved surgically by Nobel plication. Nitrofurazone therapy (0.5 Gm. twice a day) was resumed on Dec. 28 and continued until Jan. 6, 1956, when the dose was increased to 0.5 Gm. three times a day until Jan. 15 when the drug was withdrawn. The total dose administered during this period was 35 Gm. The only toxic symptoms referable to the nitrofurazone were occasional nausea and vomiting until

Jan. 14, when the patient developed severe peripheral neuritis which persisted for approximately two and one-half months and required heavy doses of narcotics for control of pain. During this period his general condition deteriorated. When the neuritis subsided, he improved markedly.

The frog test was positive on Nov. 29, 1955, before nitrofurazone therapy, but negative on Jan. 13, 1956, after administration of 33 Gm. of nitrofurazone. A chest film taken Dec. 18 showed no change in the pulmonary metastases from that of Dec. 12 (see figure, *B*), but the film obtained on Jan. 18 revealed a decrease in the density and size of several of the lesions. A film taken Feb. 24 (see figure, *C*) showed further regression in the size and density of many of the lesions, with complete disappearance of several small ones and nearly complete disappearance of a 3.5-cm. nodule in the left lower lung field. There remained only a 2.5-cm. lesion on the right and two or three smaller lesions on the left. On March 23 the lung lesions appeared to be slightly larger, and progressive enlargement of a supraclavicular node was noted. However, the patient's general condition was considerably improved and he was discharged from the hospital on April 9, 1956.

The patient was readmitted on May 9 for follow-up evaluation. Since his previous discharge, he had traveled extensively and felt well. His weight had remained constant and he had noted no gynecomastia. His only complaint was mild discomfort in the right side of his chest. A chest film on admission showed the lung metastases to be larger and slightly denser, and a frog test was positive again. Retreatment with nitrofurazone was deferred because of the severe peripheral neuritis which occurred with previous administration of the drug. The patient was discharged on May 23.

The patient was readmitted on Aug. 13, 1956, because of dyspnea, peripheral edema, bilateral chest pain, hemoptysis, and a large tender mass in the left upper part of the abdomen. A chest film taken on Aug. 28 (see figure, *D*) revealed an increase in the number and size of the metastases. The patient's condition deteriorated rapidly and on Sept. 8 hemiparesis on the left side developed. Death occurred on Sept. 12, 1956. Autopsy revealed metastases to the lungs, liver, pericardium, and regional lymph nodes. There was a massive hemorrhage of the right cerebral hemisphere, but no tumor mass.

Comment

The nitrofurans are a group of synthetic organic chemicals whose antibacterial effectiveness was first reported in 1944.[3] Over 450 nitrofurans have been synthesized, the best known being nitrofurazone (Furacin), used mainly as a topical antibacterial agent, and nitrofurantoin (Furadantin), used perorally for treatment of genitourinary tract infections and intravenously for systemic infections. Nitrofurazone was reported to delay the growth of certain experimental mouse tumors in 1948.[4] Other studies established that certain nitrofurans block spermatogenesis in rodents [5] and in man.[1c] Nitrofurazone arrests spermatogenesis at the primary spermatocyte level and causes degenerative changes in mature spermatozoa, spermatids, and secondary spermatocytes. Primary spermatocytes become rare but never disappear entirely. The spermatogonia and Sertoli cells are unaffected. The Leydig cells and androgen production remain unchanged. Recovery of the testis starts on about the sixth posttreatment day and is complete in about six weeks.

Chronic overdoses of these compounds in mice, rats, and dogs cause slight adrenocortical hypertrophy. The earliest symptoms of toxicity are nausea and vomiting, apparently due to both central and local actions. At higher dose levels neurotoxic symptoms occur. The acute oral LD_{50} of nitrofurazone in mice is from 380 to 735 mg. per kilogram of body weight.[6] Several reports indicate that orally administered nitrofurazone is safe in man at doses of 0.5 to 2.0 Gm. per day.[1] The principal toxic reactions in man have been nausea, vomiting, and severe peripheral neuritis. Chlorpromazine and enteric-coated tablets may relieve the nausea and vomiting. Narcotics, in addition to general supportive measures, may be required to control the neuritis. The dose of nitrofurazone is determined by the tolerance of the patient. In general, a daily dose of 1.25 to 2 Gm. in three or four divided doses has been used.[1b]

Summary and Conclusions

A 35-year-old patient with a teratocarcinoma of the testis developed pulmonary metastases after orchiectomy, radical retroperitoneal node dissection, and x-ray therapy. Nitrofurazone (Furacin) was administered perorally to a total dose of 35 Gm. over a period of six weeks. The pulmonary metastases decreased markedly in number and size for a period of several months. The clinical response was difficult to evaluate owing to the occurrence of a severe peripheral neuritis. Death with recurrent pulmonary metastases and cerebral hemorrhage occurred nine months after the course of nitrofurazone.

It is concluded that nitrofurazone should be given further trial in the treatment of testicular tumors. This drug may also be useful preoperatively and in conjunction with irradiation to control or eradicate metastases of testicular tumors.

1055 Clermont St. (20) (Dr. Elrick).

The nitrofurazone used in this study was supplied as Furacin by the Eaton Laboratories, Norwich, N. Y.

References

1. (*a*) Friedgood, C. E., and Ripstein, C. B.: Effect of Nitrofurazone on Tumors of Human Testis, and Prostate Gland, S. Forum (1951) pp. 329-333, 1952. (*b*) Wildermuth, O.: Testicular Cancer: Management of Metastases, with Report of New Chemotherapeutic Agent, Radiology **65:**599-603 (Oct.) 1955. (*c*) Friedgood, C. E.; Danza, A. L.; and Boccabella, A.: Effects of Nitrofurans on Normal Testis and on Testicular Tumors (Seminoma) abstracted, Cancer Res. **12:**262-263 (April) 1952.

2. References 1*a* and *c*.

3. Dodd, M. C., and Stillman, W. B.: In Vitro Bacteriostatic Action of Some Simple Furan Derivatives, J. Pharmacal. & Exper. Therap. **82:**11-18 (Sept.) 1944.

4. Green, M. N., and Friedgood, C. E.: Action of Furacin in Delaying Growth of Transplanted Fibrosarcoma in Mice, Proc. Soc. Exper. Biol. & Med. **69:**603-604 (Dec.) 1948.

5. Prior, J. T., and Ferguson, J. H.: Cytotoxic Effects of Nitrofuran on Rat Testis, Cancer **3:**1062-1072 (Nov.) 1950. Nelson, W. O.; Steinberger, E.; and Boccabella, A.: Recovery of Spermatogenesis in Rats Treated with Nitrofurans, abstracted, Anat. Rec. **118:**333-334 (Feb.) 1954.

6. Krantz, J. C., Jr., and Evans, W. E., Jr.: Contribution to Pharmacology of 5-Nitro-2-Furaldehyde Semicarbazone, J. Pharmacol. & Exper. Therap. **85:**324-331 (Dec.) 1945. Giarman, N. J.: Antibiotic Lactones and Synthetic Analogs: III. Efficacy in Experimental Trypanosomiasis, ibid. **102:** 185-195 (July) 1951.

FARMER'S LUNG

AN ACUTE GRANULOMATOUS INTERSTITIAL PNEUMONITIS OCCURRING IN AGRICULTURAL WORKERS

Helen A. Dickie, M.D.
and
John Rankin, M.D., Madison, Wis.

Farmer's lung is a potentially serious and crippling disease that results from handling a variety of dusty, moldy organic materials. The symptoms are shortness of breath, cough, fever, chills, weight loss, and hemoptysis. This condition differs from silo filler's disease in both causation and symptoms. The roentgenographic findings are those of interstitial pneumonitis. Biopsy of the lung reveals a granulomatous interstitial pneumonitis with epithelioid and giant cells. This report is based on 39 cases. Lung biopsies were done in eight, and two cases are described in detail. Repeated exposure was followed by recurrence. No causative organism was found. A given exposure induced the disease in some persons while leaving others unaffected. Individual hypersensitivity to molds or to their products seemed to be a decisive factor. Antibiotic therapy is not primarily indicated. The essential treatment is for the patient to avoid repetition of the exposure.

During the past several years, we have encountered, with increasing frequency, a peculiar respiratory illness among farmers who have been exposed to moldy forage. This disease is a distinct, easily recognized clinical syndrome with uniform clinical, roentgenographic, physiological, and pathological features. It is, we believe, an important hazard to agricultural workers, which is not related to the recently described, superficially similar, but much less frequently encountered silo-filler's disease.[1] The purpose of this report is to document the major features of this syndrome so that it may receive the attention which we believe it deserves.

During the past eight years, 36 men and 1 woman have been seen at the University Hospitals and 2 additional men have been seen at the Madison Veteran's Administration Hospital on account of respiratory difficulties of varying severity. The duration of symptoms varied from three days to 10 years, but the average patient had had recurrent difficulties for approximately 3 years. All had received prior medical attention, and one-half had been hospitalized elsewhere one or more times. Their ages varied from 12 to 65 years. Two were between 10 and 20 years of age, 6 between 21 and 30, 9 between 31 and 40, 10 between 41 and 50, 10 between 51 and 60, and 2 between 61 and 70. All but two were life-long farmers, and it seems clear that the disease appeared only after many years of farming experience.

The onset of the acute illness followed exposure to various dusty jobs on the farm. Only two individuals were uncertain about the presence of mold in the dust thought to be responsible for the attack. The type of dusty material handled by others prior to the onset of their first acute episode included moldy hay, fodder, and grain, 19; moldy silage, 11; moldy shredding or threshing dusts, 6; and moldy tobacco, 1. Moldy hay, grain, fodder, and silage were thus the most frequent offenders, while the dusty atmosphere associated with threshing and shredding was also felt to be an offending agent. Exposure usually occurred within a closed bin, silo, or barn where ventilation was poor.

From the Department of Medicine and the Cardiopulmonary Laboratory, University of Wisconsin.

Read before the Medical Session of the Annual Meeting of the American Trudeau Society, Kansas City, Mo., May 6, 1957.

Clinical Features and Laboratory Findings

Clinical Features.—In most instances, exposure to a dusty job was followed within a few hours by chills, fever, cough, and shortness of breath. A few patients had experienced some minor symptoms, such as chills, headache, or malaise, when in contact with the offending dusts prior to the exposure which produced the alarming respiratory difficulty.

The major symptoms of the entire group were as follows: Shortness of breath was a constant complaint (39, or 100%). This was noted by most of the affected individuals during the acute febrile episode. In some, there was alarming dyspnea, frequently associated with cyanosis. More commonly, the patient's original illness was such that the acute malaise, fever, and chills were more striking, and only when this acute episode subsided and the farmer attempted to return to his ordinary farm work did he realize that he became very short of breath on the slightest exertion. This sharp limitation of ability to perform work persisted for several weeks after an acute febrile episode. Cough

was present in all but a 12-year-old boy (38, or 97%). The cough was a harassing one which occurred at the onset of the acute illness and persisted for several days without the patient having further contact with the moldy material. The chronicity of the cough, as well as other symptoms, was frequently difficult to determine because the individual usually returned to the dusty environment. Fever was likewise a very common symptom (38, or 97%), and, in many individuals, actual temperature elevations to 104 to 106 F (40 to 41.1 C) were recorded. Associated with the fever was a generalized malaise and severe headache. Severe shaking chills were frequent (33, or 85%), as well as the less dramatic sensation of chilliness.

Weight loss of 10 to 20 lb. (4.5 to 9.1 kg.) was common in this group of men who usually were not

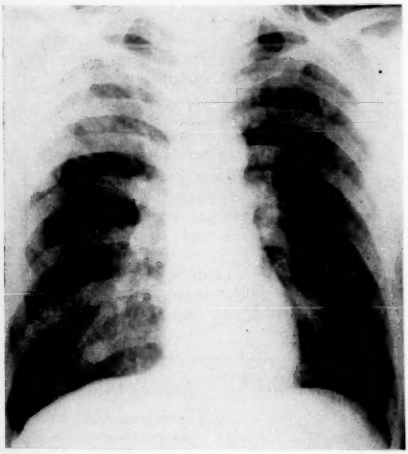


Fig. 1.—Chest roentgenogram showing most characteristic evidence of farmer's lung: interstitial pneumonitis.

overweight at the time of their illness (29, or 88%; not recorded in 6). The sputum was usually neither copious nor very purulent. Although two patients had experienced frank hemoptysis, the usual description of the bleeding episode was that of blood-streaked sputum (10, or 26%). Tightness of the chest was a common symptom, but a pleural type of pain was seen in only one individual, who developed cough fractures of the ribs. The patients were usually free of symptoms during the summer, when stored forage was not being used, but had recurrent difficulties during the winter months.

In this type of illness, the problem of an allergic diathesis of the patient must be considered. A familial history of some recognized illness frequently associated with an allergic state was obtained in nine, or about one-fourth of the group. Only five patients gave any history of a previous illness suggesting an allergy. Three patients had previously had asthma and hay fever, and one had previously noted hay fever during the height of the ragweed season. Another patient suffered from "chronic sinusitis." All of the asthmatic patients were convinced that the type of shortness of breath, even in the acute episodes, was distinct from the respiratory distress they had previously noted in their asthmatic attacks.

The abnormalities that could be demonstrated on physical examination of these patients varied considerably, according to the severity of their illness. It was noteworthy that the acutely ill, frequently cyanotic, febrile patient did not appear as critically ill or suffering with as severe a toxic reaction as the usual patient with pneumonia who had a comparable degree of respiratory embarrassment and cyanosis. Numerous crepitant rales, without evidence of consolidation and without the wheezing and obvious expiratory effort noted in the patient with an acute asthmatic attack, was the usual finding. Breathing was shallow and rapid. These patients resisted anything that would increase the respiratory excursion, because of the severe cough that resulted. In the less severely ill patient, numerous fine crepitant rales at the end of a forced inspiration were the most constant finding. These rales persisted long after the chest roentgenogram had returned to a normal appearance. Forced expiration frequently resulted in the finding of a few high-pitched squeaks, suggesting involvement of the finer divisions of the bronchial tree.

Laboratory Findings.—Sputum examinations for fungi were done in 30 of the 39 patients. Of these, 16 patients' sputums revealed Candida albicans, 1 C. parakrusei, and 1 Aspergillus. An incidence of C. albicans in approximately 50% of the sputums in a group of patients who nearly all had previously had antibiotic therapy is of uncertain significance.

A polymorphonuclear leukocytosis, with counts varying from 11,000 to 22,000 per cubic millimeter, was found in 10 of the 39 patients. All were having an acute episode and were still febrile. Eosinophilia was observed in 6 of the 39 patients, and the eosinophil level varied from 5 to 16%. It is possible, too, that this eosinophilia was due to prior antibiotic therapy, especially that with streptomycin sulfate. Only five individuals revealed a slight increase in the total red blood cell count, hemoglobin level, and hematocrit value. This was so slight as to be of doubtful significance.

Chest Roentgenograms, Pulmonary Function Studies, and Pathology

Chest Roentgenograms.—The chest roentgenograms varied considerably with the severity and the duration of the illness. Extensive interstitial changes so marked that the radiologist suggested

the diagnosis of an "azotemic lung" were seen in one acutely ill patient. The usual finding, however, was a diffuse interstitial pneumonitis with varying degrees of patchy pneumonic densities (fig. 1).

These more conglomerate densities tended to clear within a week or two, but peribronchial accentuation persisted for at least a month or even longer. In the more chronically involved patient who had repeated episodes, fibrotic stringy densities appeared and cleared slowly, if at all. Right pleural thickening of considerable degree developed in one patient who was followed for eight years. It is important to recognize that a normal appearance of the chest roentgenogram does not exclude the diagnosis of farmer's lung. Among the patients for whom lung biopsies were done, the immediately preoperative chest roentgenograms were interpreted as having returned to normal in two patients but the lung biopsies in both instances revealed an acute granulomatous interstitial pneumonitis. The complaints of dyspnea on exertion persisted after the roentgenographic evidence of an acute interstitial pneumonitis had disappeared.

Pulmonary Function Studies.—Space does not permit more than a brief summary of the physiological abnormalities that may be present. During the acute episode of pneumonitis, there may be severe hypoxia of arterial blood, which is the result of a striking reduction in pulmonary diffusing capacity and abnormality in the relationship of ventilation and pulmonary blood flow. When the patient is well enough to tolerate more extensive pulmonary function studies, there is found to be hyperinflation of the lungs with a significant increase in residual volume and functional residual capacity and a moderate reduction in vital capacity. The moderate reduction in maximum breathing capacity, timed vital capacity, and expiratory air flow rates confirm the clinical impression of obstruction in the small bronchi or bronchioles.

Pathology.—Surgical biopsies of the lung were done in eight patients. In six, the abnormality noted was an acute granulomatous interstitial pneumonitis consisting chiefly of epithelioid cells and a few giant cells. A few well-formed tubercles were present. In two patients, these changes were not seen. In one (case 2), the lesion was that of an interstitial fibrosis which was consistent with a history of repeated difficulties for eight years prior to the taking of this biopsy. In the other patient, the granular nodular densities had cleared almost completely. The only abnormality noted was fibrosis of the lung with patchy collections of lymphocytes. No epithelioid or giant cells were noted. This patient had a characteristic history and an interstitial pneumonitis, which cleared slowly. It is possible that the biopsy was made in an area previously involved, since he had a history of pneumonia in 1940 and the pleural space was obliterated by adhesions at the time of the surgical biopsy. The smears and cultures of these lung specimens did not reveal fungi or tubercle bacilli. There was no evidence of caseation necrosis noted in any of the specimens.

Report of Cases

Case 1.—A 22-year-old man, a farmer, was admitted April 23, 1956, because of cough and shortness of breath for one year. He had enjoyed excellent health until late in the spring of 1955, when he baled old hay which was covered with a white mold and was very dry and dusty. This work was done in the morning, and by that afternoon he noted shortness of breath, weakness, chills, fever, a tight feeling in his chest, and an irritating, nonproductive cough. He was hospitalized at his local hospital for four days and was treated with penicillin and sulfonamides because of the roentgenographic evidence of pneumonia. After one week, he was able to work and felt quite well.

On the morning of Aug. 20, 1955, he removed spoiled, moldy, grass silage which had been stored in the silo early in July, 1955. By that afternoon, he had symptoms entirely similar to those noted previously. He was hospitalized for nine days. The diagnosis was "virus pneumonia." During

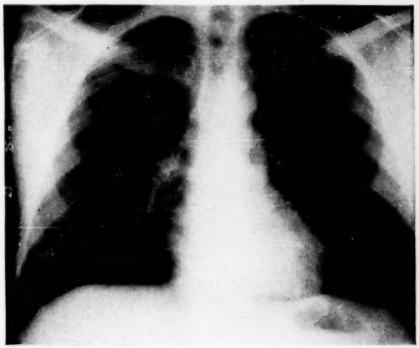


Fig. 2 (case 1).—Chest roentgenogram just prior to biopsy of lung.

this illness, he lost about 20 lb. (9.1 kg.). By Sept. 15, 1955, he returned to work but observed dyspnea when doing any heavy work. On Jan. 1, 1956, he developed a "head cold," characterized by nasal discharge, malaise, slight fever, and headache. After one week, a cough which was productive of a small amount of "yellow phlegm" was noted, accompanied by shortness of breath and anorexia. Chills and fever were intermittent, and he did not seek medical attention until Feb. 1, 1956, when he was hospitalized and treated with antibiotics for pneumonia and bronchitis. After three days, he was discharged but never "felt up to par." Chills, fever, and night sweats continued. Dyspnea occurred on climbing one flight of stairs, and he complained of palpitation on exertion. He was hospitalized for eight days, was treated with tetracycline, and felt improved. When he returned to his work, he again experienced chills, fever, and night sweats. On closer questioning, it was evident that at the time of the recurrence of his symptoms on Jan. 1, 1956, he had again worked with the grass silage which had been handled prior to the episode on Aug. 20, 1955. Although his father had worked with the same silage, he had experienced no illness.

The physical examination revealed a large, muscular young man who did not appear ill. A few fine inspiratory rales were heard at both bases. The chest roentgenogram (fig. 2) revealed minimal peribronchial changes. Chest roentgenograms taken in June, 1955, had shown minor interstitial changes. On March 2, 1956, there was a definite interstitial change most marked at the left lung base. This had cleared considerably by March 9, 1956. Biopsy of the lung revealed the characteristic granulomatous interstitial changes (fig. 3).

CASE 2.—A 35-year-old man, also a farmer, was first seen as an outpatient on March 20, 1950. He reported that he had ceased smoking in November, 1949, because of a cough which was sudden in its onset. He had fever with temperatures as high as 102 F (38.8 C) and raised yellow sputum, which gradually increased in amount. Shortness of breath when he attempted to do any work was very troublesome. Recurrent episodes of fever, chills, and severe headache continued to occur about once a week. After four to five hours,

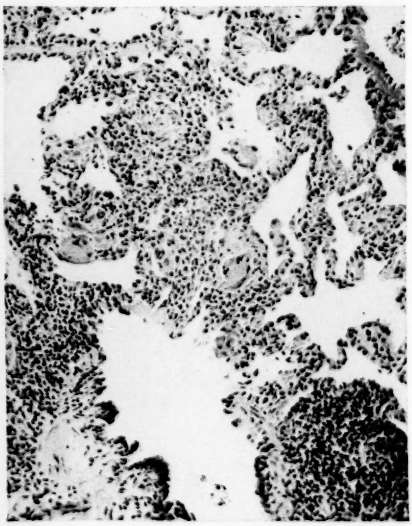


Fig. 3 (case 1).—Photomicrograph of lung section, revealing characteristic granulomatous interstitial reaction (× 150).

he experienced a malodorous sweat. Between these episodes, he felt quite well. He had lost 25 lb. (11.3 kg.) since November, 1949. Fortunately, his wife, who accompanied him, was an observant individual. She volunteered the information that his periods of illness had always recurred when he felt well enough to return to doing his farm chores. The history was then obtained that, when he was working with moldy silage in 1946 or 1947, he had noted fever and headache after handling it but was not aware of any respiratory complaints. Before the illness in November, 1949, he had worked with moldy millet hay, and he had been working with the same material each time he had chills and fever. His brother, who had worked with the same moldy silage and hay, had suffered no ill-effects. Penicillin injections in February, 1950, had produced no benefit. The physical examination revealed fine crepitant rales at both bases. The blood cell count was normal. Agglutination tests for Brucella abortus were negative. Sputum cultures revealed Candida albicans. The chest roentgenogram showed the cardiac silhouette to be normal. There was a generalized loss in aeration in the lung fields, most pronounced at the lung bases. The diaphragms were smoothly rounded with clear sulci. A diagnosis of farmer's lung was made, and the patient was advised to avoid all contact with barn dusts.

In December, 1950, he was seen again. He reported that he had gained weight and that during the summer he had been well and had been able to do his regular farm work. In mid-October, 1950, his cough recurred and blood-streaked sputum was observed. Fever and night sweats were present. He had been working in the barn but had not been handling any moldy hay. On physical examination, numerous rales were present, especially at the right lung base. Chest x-ray on Dec. 15, 1950, showed clearing of the interstitial changes. There was a small homogeneous density at the right cardiohepatic angle. A distinct change in the cardiac silhouette was seen. There was a prominent convex bulge in the left midcardiac border. The allergy consultant found the patient to show slight reactions to tree and ragweed pollen and to stockhouse dust and barn dust. Desensitization with house and barn dust was recommended. On Feb. 12, 1951, a chest x-ray showed no clearing of the right lung changes. Cardiac fluoroscopy was done, and the prominence of the left cardiac border was believed to be explained by pleuropericardial adhesions. A bronchogram of the right lung was done because of the clinical suspicion of bronchiectasis, but the bronchial tree was found to be normal. Sputum cultures showed no fungi at this time.

In February, 1954, a note was received from a local sanatorium that the patient had been seen there because of extensive bilateral disease suggestive of tuberculosis but that tubercle bacilli could not be found on culture of sputum or gastric aspirate. In March, 1955, he was admitted to the Madison, Wis., Veterans Administration Hospital because of progressive difficulty. He was no longer able to work full time but had remained on the farm. He continued to cough and expectorate as much as one cup of sputum per day. The sputum had been blood-streaked on many occasions. There had been a weight loss of 22 lb. (10 kg.). Chest pain on the right side had been present during several of his more recent episodes of chills and fever. Increased shortness of breath had been a major factor in limiting his working ability.

On physical examination, he appeared to be acutely and chronically ill. Dyspnea occurred with the effort of sitting up. Numerous rales were heard, especially over the right lung. The heart was not enlarged. The pulmonic second sound was accentuated. The total blood cell count was normal. Numerous sputum studies showed no fungi or tubercle bacilli. Pleural thickening on the right side, obliterating the sulcus, and strands of fibrosis in the right upper lung field were the major changes seen in the chest roentgenogram (fig. 4). There were some granular nodules, chiefly in the lower lobes. The left lung revealed similar but less marked changes. On April 13, 1955, a bronchogram was done on the right side. There was considerable distortion of the bronchi and moderate cylindrical dilation of the medial basal segmental bronchi. A bronchoscopy was done April 12, 1955. The trachea was deviated to the right. Moderate redness and thick fibrinous exudate was observed in the right main stem bronchus. The lobar bronchi appeared normal. Cardiac catheterization revealed normal findings. On June 21, 1955, a surgical biopsy of the right lung was done (fig. 5). The pleural space was obliterated by adhesions. The lung specimen revealed a pleural thickening, fibrosis of the alveolar walls, and peribronchial fibrosis. No epithelioid or giant cells were found.

These two patients demonstrate very clearly the recurrent episodes of rather serious illness. Subsequent observation has shown, fortunately, that the

younger man seems to be very little handicapped, since he has avoided continued exposure to the noxious materials. The second man originally had the same type of symptoms, but after continued exposures for eight years he reached the point of having marked permanent lung damage.

Comment

The diagnosis of farmer's lung requires an awareness of this illness. The evidence of the dust exposure, usually with moldy material, in the patient's history is not difficult to elicit. However, as such exposure is very common and frequently has been tolerated by the individual previously, he may not attach any significance to this. To complicate the problem further, many patients fail to recognize the possible correlation because their co-workers have suffered no ill-effects. Also, respiratory symptoms in the winter months and freedom from difficulty in the summer months may be interpreted as being due to recurrent respiratory infections. However, in this study a detailed occupational history usually demonstrated a close correlation between the exposure to dust and the onset of chills, fever, cough, headache, and shortness of breath within a few hours.

The differential diagnosis between this type of illness, usually termed farmer's or thresher's lung, and the more recently described silo-filler's disease [1] is not difficult to make in the usual patient. The latter illness is due to nitrogen dioxide irritation of the respiratory tract. These noxious fumes are created by the fermentation of nitrates in the forage placed in the silo. The period of production of these noxious gases fortunately is a transient one, usually starting within a few hours and not lasting more than 10 days to two weeks. There has been much attention directed to this hazard, so that most farmers are aware of the possible dangers.

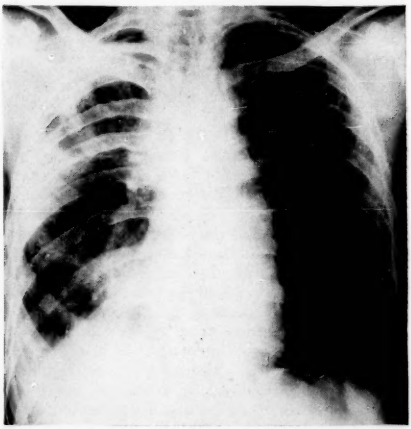


Fig. 4 (case 2).—Chest roentgenogram seven years from onset of illness. Marked pleural fibrosis is more evident than scattered stringy nodular densities in lung fields.

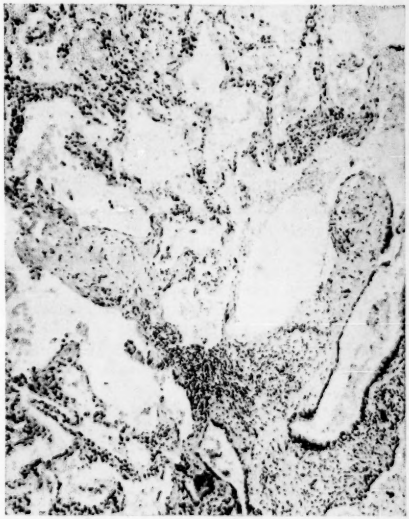


Fig. 5 (case 2).—Photomicrograph of lung section, showing alveolar walls moderately thickened and fibrous. No epithelioid or giant cells are seen (× 75).

The gas is usually concentrated enough to be primarily irritant, so that the person has to leave the area promptly. Occasionally, a concentration may be present that is strong enough to cause immediate death. If the concentration is lower, the onset of symptoms may be delayed. The acute episode may be indistinguishable clinically and roentgenographically from farmer's lung. Autopsy and biopsy reports show acute edema in the fulminating cases and subacute bronchopneumonia with bronchiolitis fibrosa obliterans in the chronic cases. The latency between exposure to these gases and the development of the acute respiratory symptoms apparently depends on the concentration of the gases, as several patients have died within a few hours. In our experience, this is a much more uncommon illness than that seen secondary to contact with the moldy silage when the silo is opened for the first time and the large amount of mold is present. The history concerning the date of the silo filling, as well as the frequent recognition by the affected person that there was an unusual gas present, will clarify the diagnosis.

The incidence of farmer's lung is a difficult problem to assess. However, we believe it to be much more common than a report of 39 patients would suggest. Many patients have minor episodes of this type of illness without recognition of the true nature of the illness. With the acute onset of chills, fever, and cough, supported by physical evidence of rales in the lung fields, pneumonia is a common diagnosis. Among older patients, the symptoms of dyspnea on exertion coupled with evidence of fine rales at both bases frequently lead to an erroneous diagnosis of cardiac failure. Repeated bouts of chills and fever without marked respiratory complaints suggest the possibility of brucellosis in a farmer. Bronchiectasis is frequently suspected. In several patients in this study, bronchograms were done because of this suspicion, but no bronchial abnormality was demonstrated except in the second bronchogram done on the patient in case 2.

On the whole, failure to establish the proper diagnosis during the initial acute illness will seldom impair the patient's chances of recovery from this episode, for most of these patients improve when they are removed from the offending dusts. The patient may, of course, have been subjected to unnecessarily prolonged hospitalization, costly laboratory investigations, and therapy with expensive antibiotics. Of more importance, however, is the fact that if the proper diagnosis is not made the farmer is likely to be reexposed to the offending agent. In some persons, this may produce alarming and potentially fatal acute pulmonary insufficiency. More commonly, continued reexposure results in a chronic inflammatory reaction in the lung or numerous subacute episodes of interstitial pneumonitis which ultimately produce permanent and totally incapacitating pulmonary insufficiency. The economic problems created by this illness are major ones, as the farmer usually has to leave the farm or hire help to do the work in dusty areas. As would be expected, there is a great reluctance on the part of these individuals to give up farming until they are forced to do so because of their inability to do the work. By this time, their pulmonary damage is usually so great that any manual labor, even in a dust-free environment, is not well tolerated. In our opinion, this disease would attract much more attention if it occurred in an industrial group where there is a greater concentration of individuals and where the problem of compensation might be raised.

Treatment of these patients has not been uniform, due in part to the wide variation in the clinical symptoms. The removal of the patient from further contact with the offending material is most important in the control of the symptoms. In the acutely ill patient, this is accomplished by his own illness. Unless there has been a very severe degree of pulmonary involvement, the patient frequently feels much better and the acute fever, as well as the cough, subsides after three to seven days. This fact has frequently led to the erroneous conclusion that the patient's "pneumonia" has responded to antibiotic therapy. However, the persistence of dyspnea on exertion is unlikely after bacterial pneumonia. In the acutely ill patient, steroids have been utilized with apparent benefit, although evaluation is difficult. In the patient who has persistent dyspnea and clinical evidence indicating residual interstitial pneumonitis, adrenal steroids have been utilized with marked subjective improvement in the disabling shortness of breath. The mode of action of adrenal steroids is undoubtedly complex, but suppression of tissue hypersensitivity, which we believe underlies the inflammatory phenomena, is a reasonable hypothesis. Also, adrenal steroids have been shown to be of value in other forms of pulmonary granulomatosis and in various diseases thought to result from tissue hypersensitivity. It appears logical to utilize them in an attempt to shorten the duration of disability and to lessen the residual damage. In our experience, iodides have been of little value.

The etiology of farmer's lung remains unsolved. In 1932, Campbell [2] presented a brief clinical report of a peculiar respiratory illness in five farmers seen in the months of April and May, 1932. The severity of their illness, which was associated with contact with "white mold" on hay and grain, prompted this excellent clinical description. He noted that the wet summer of 1931 had created an unusual amount of moldy grain and hay in Westmorland. Later, Fawcitt,[3] also of northwest England, published several articles on the same peculiar respiratory illness. He concluded that the disease was an actual mycotic infection of the bronchi.

In 1945, Duncan,[4] in a general discussion of fungus disease in Great Britain, commented on farmer's lung. He did not agree that this was a true mycotic infection. He questioned whether the mold in its growth on the hay produced some noxious substances or whether the mold, by breaking down the hay fibers, produced a sufficiently fine vegetable dust to cause, by inhalation, a disorder analogous to byssinosis of cotton-mill workers. He favored the latter concept.

Törnell,[5] in Sweden, reported on eight patients with the same type of illness who had been exposed to moldy grain in the threshing process. He used the term thresher's lung and concluded that these individuals actually had moniliasis of the bronchial tree.

Zettergren,[6] in 1950, reported on animal studies. Rabbits were exposed in a dust chamber for one hour for 10 successive days. Twenty rabbits (series A) were exposed to sterile threshing dusts, and 28 rabbits (series B_1 and B_2) were exposed to sterile threshing dusts mixed with viable Candida (Monilia) albicans. Series A and B_1 were sacrificed

five days after the exposure was completed and those in Series B_2 10 weeks after exposure. Inhalation of sterile dusts caused submiliary histiocytic lung granulomas, which Zettergren labeled dust granulomas. With C. albicans added, submiliary-miliary tuberculoid granulomas (fungal granulomas) were found. The dust granulomas were of shorter duration than the fungal granulomas. The fungi did not multiply in the rabbit's lung.

Studdert,[7] in 1953, described four patients with farmer's lung. In his discussion, he expressed doubt as to the actual fungus infection and concluded that farmer's lung represented a nonspecific irritant, probably a foreign protein. In the same year, Fuller's review[8] of farmer's lung appeared. In eight years, he had collected 32 cases. He described three phases of the disease: "(1) the acute isolated attack, (2) the subacute and more chronic condition which shows a spontaneous tendency to recover, and (3) the chronic and irreversible phase where secondary lung changes such as emphysema and fibrosis have occurred as the result of repeated exposure over a period of years." He concluded that farmer's lung is the result of irritation of the bronchial epithelium by the breakdown of mold spores and possibly grass particles.

Soucheray,[9] in 1954, reported on three patients with farmer's lung. He suggested that farmer's lung was pulmonary moniliasis. In 1956, Williams and Mulhall[10] reported on 10 patients from Wales. They suggested that the respiratory difficulty is due to a plugging of the terminal parts of the bronchial system by the mold spores.

In addition to the reports of farmer's or thresher's lung, other reports of exposure to dust have appeared which seem comparable in clinical and roentgenographic descriptions. In 1932, Towey and co-workers[11] reported on 35 patients whose illness was believed due to the spores of a fungus tentatively identified as Coniosporium corticale, found in maple bark. Their concept of the pathogenesis of this illness is well stated in their summary: "It is our opinion that this illness is due to a local toxic effect and foreign body reaction combined with a delayed effort resembling protein sensitization in its clinical and certain immunologic aspects."

The illness reported by several authors[12] occurring among workers exposed to the sugar cane residual fiber, bagasse, is similar in clinical and roentgenographic pattern. Castleden and Hamilton-Paterson[12b] suggested that the acute phase was an allergic response. However, in the report of Sodeman and Pullen,[12c] the description of the needle biopsy of the lung in their patient and of the lung section from another patient who died with this disease is not that of an acute granulomatous interstitial pneumonitis. They reported an increase in the fibroblastic reaction of the interstitial cells. On examination with polarized light, small spicules were noted. In the needle biopsy specimen, a large piece of foreign material with the appearance of bagasse was noted.

In our opinion, farmer's lung is caused by the sensitization of the individual to the molds or the product of these molds. The causal relationship between the exposure to the moldy material and the illness seems evident. The exact role of the molds, dust, and individual susceptibility remains unknown. The onset of chills and fever within a few hours after exposure to the suspected noxious material is quite unlike the usual response to fungus infection of the lungs. The diffuse interstitial pneumonitis is not the pattern associated with some other fungus infections due to inhalation of the spores, namely, histoplasmosis and coccidioidomycosis. The clinical picture of chills, fever, and cough resembles much more closely that observed with the inhalation of tuberculoproteins in the individual who is sensitive to tuberculin. The microscopic changes in the lung are similar to changes noted in other conditions currently regarded as a tissue hypersensitivity response. Studies to clarify these factors are not simple because of the great complexity of the molds and the variation of the organic material, as well as the selection of a suitable experimental animal. The creation of a sensitivity prior to the "dusting" that might produce a pattern similar to the clinical disease is another problem.

At the present time, prevention of exposure seems to be the only logical course. It should be stressed to agricultural workers that these moldy materials are hazardous. If acute illness does not occur, it does not mean that the patient has not developed a sensitivity.

In Wisconsin, there is a greater chance for the development of farmer's lung than in many areas of the United States. The major farm activity is dairying. This requires the storage of a large amount of hay and grain for cattle feed. Climatic conditions which favor poor drying are common. The hay and grain are usually stored in poorly ventilated mows and bins. Once moldy hay has been in the mow, the area may remain contaminated for years, since the mows are rarely entirely emptied and cleared of the residual moldy material. Severe winters have resulted in the construction of relatively air-tight barns, which cause a higher and more prolonged dust concentration than would be present where feeding is done in the open lot or shed. In addition to these factors, silos are widely used for the production of corn and, more recently, grass silage. This material is frequently moldy on the top and edges when the silo is first opened. The dry, very dusty, moldy

silage is tossed down the chute, and, frequently, the only source of air is from this chute. The dust concentration can be extreme.

Farmers must recognize the hazard and make every attempt to prevent the storage of wet material which will produce mold. The development and wider use of driers may be helpful in the control of this problem. If material has become moldy, then use of effective masks and even wetting down of the usually very dry and extremely dusty moldy material prior to handling must be considered. If the farmer realizes that the handling of moldy material may be a hazardous as well as a disagreeable task, farmer's lung may be seen less frequently.

Summary

Thirty-nine patients with farmer's lung were seen, and lung biopsy was done in eight patients. Six specimens revealed a granulomatous interstitial pneumonitis with epithelioid and giant cells.

Symptoms of shortness of breath, cough, fever, chills, weight loss, and hemoptysis occurring in individuals exposed to organic dusts should arouse the suspicion of farmer's lung. The roentgenographic evidence of an interstitial pneumonitis in patients with these complaints makes the diagnosis of farmer's lung almost certain. Farmer's lung is a potentially serious and crippling disease, believed possibly to result from a hypersensitivity response to molds or the products of molds occurring in a wide variety of organic material.

1300 University Ave. (6) (Dr. Rankin).

This study was supported by a grant from the Wisconsin Heart Association.

References

1. Delaney, L. T., Jr.; Schmidt, H. W.; and Stroebel, C. F.: Silo-Filler's Disease, Proc. Staff Meet. Mayo Clin. **31**:189-198 (April 4) 1956. Lowry, T., and Schuman, L. M.: "Silo-Filler's Disease"—Syndrome Caused by Nitrogen Dioxide, J. A. M. A. **162**:153-160 (Sept. 15) 1956. Grayson, R. R.: Silage Gas Poisoning: Nitrogen Dioxide Pneumonia, New Disease in Agricultural Workers, Ann. Int. Med. **45**:393-408 (Sept.) 1956.

2. Campbell, J. M.: Acute Symptoms Following Work with Hay, Brit. M. J. **2**:1143-1144 (Dec. 24) 1932.

3. Fawcitt, R.: Fungoid Conditions of Lung: I., Brit. J. Radiol. **9**:172-195 (March) 1936; Fungoid Conditions of Lung: II., ibid. **9**:354-377 (June) 1936; Occupational Diseases of Lungs in Agricultural Workers, ibid. **11**:378-392 (June) 1938.

4. Duncan, J. T.: Survey of Fungous Diseases in Great Britain: Results from First Eighteen Months, Brit. M. J. **2**:715-718 (Nov. 24) 1945.

5. Törnell, E.: Thresher's Lung: Fungoid Disease Resembling Tuberculosis or Morbus Schaumann, Acta med. Scandinav. **125**:191-219 (Aug.-Sept.) 1946.

6. Zettergren, L.: Thresher's Lung (Pulmonary Moniliasis): Experimental Investigation, Upsala Läkaref. förh. **55**:257-313 (Dec.) 1950.

7. Studdert, T. C.: Farmer's Lung, Brit. M. J. **1**:1305-1309 (June 13) 1953.

8. Fuller, C. J.: Farmer's Lung: Review of Present Knowledge, Thorax **8**:59-64 (March) 1953.

9. Soucheray, P. H.: Farmer's Lung: Form of Bronchopulmonary Moniliasis, Minnesota Med. **37**:251-253 (April) 1954.

10. Williams, D. I., and Mulhall, P. P.: Farmer's Lung in Radnor and North Breconshire, Brit. M. J. **2**:1216-1218 (Nov. 24) 1956.

11. Towey, J. W.; Sweany, H. C.; and Huron, W. H.: Severe Bronchial Asthma Apparently Due to Fungus Spores Found in Maple Bark, J. A. M. A. **99**:453-459 (Aug. 6) 1932.

12. (*a*) Jamison, S. C., and Hopkins, J.: Bagasscosis: Fungus Disease of Lung: Case Report, New Orleans M. & S. J. **93**:580-582 (May) 1941. (*b*) Castleden, L. I. M., and Hamilton-Paterson, J. L.: Bagassosis: Industrial Lung Disease, Brit. M. J. **2**:478-480 (Oct. 24) 1942. (*c*) Sodeman, W. A., and Pullen, R. L.: Bagasse Disease of Lung, New Orleans M. & S. J. **95**:558-560 (June) 1943.

A DISCOVERY OF THE FIRST MAGNITUDE.—I believe that the finding of Fraenkel-Conrat and Gierer and Schramm that virus activity may reside in a nucleic acid represents a discovery of the first magnitude, for it means that a polynucleotide of comprehendible structural complexity can carry the code of informational pattern not only for the production of more of the same polynucleotide but also for the de novo production of a highly specific polypeptide. It provides a much more sound experimental as well as theoretical base for contemplating the existence of the myriads of living things on earth. It is a discovery that is affecting the thinking and the course of events in virus research and all that virus research is concerned with, such as genetics, infectious disease, cancer and life itself. Eventually chemists should be able to synthesize a small polynucleotide specifically arranged, hence one may now dare to think of synthesizing in the biochemical laboratory a structure possessing genetic continuity and of all the tremendous implications of such an accomplishment. Studies of this nature and related studies could easily lead directly to the heart of the cancer problem and provide a solution to a situation which today appears so very perplexing.—W. M. Stanley, The Potential Significance of Nucleic Acids and Nucleoproteins of Specific Composition in Malignancy, *Texas Reports on Biology and Medicine*, Fall, 1957.

THE WESTERN RESERVE ANESTHESIA MACHINE, OXYGEN INHALATOR, AND RESUSCITATOR

Robert A. Hingson, M.D., Cleveland

Anesthesia can be induced quickly and maintained for periods of 3 to 20 minutes in obstetric, pediatric, dental, and traumatic cases by administering cyclopropane with helium and oxygen from thumb-sized cylinders. The mixture of 30% oxygen, 30% helium, and 40% cyclopropane is nonexplosive. Administration is accomplished by an easily portable machine here described. This midget type of anesthesia machine has been used to anesthetize more than 8,500 patients in the course of five years. It has also been uses successfully in asministering oxygen in units of 3,400 cc. for resuscitation or for brief periods of oxygen therapy. Because of its simplicity the machine is easily refilled or disassembled for cleaning. Clinical experience and laboratory data have shown it to be safe and effective when properly used.

Since 1933 cyclopropane as an anesthetic, introduced by Ralph Waters at Madison, Wis., has assumed an ever-increasing place in anesthesiology. The fact that this agent is flammable has limited its use in many small hospitals, operating rooms, and physicians' offices, where conditions did not permit costly explosion prevention.

In March, 1953, members of our Western Reserve University department of anesthesia, department of chemistry, research medical students in the new educational phase program, a professor of physics of Case Institute, and the engineering department of a Cleveland manufacturing company combined forces and efforts to package an instantaneous nonexplosive anesthetic mixture containing 30% oxygen, 30% helium, and 40% cyclopropane, or 100% oxygen if required for inhalation or resuscitation.[1] These mixtures are packaged in thumb-sized cylinders, especially adapted for a small, 2-lb. aluminum anesthesia machine,[2] which can serve also as an oxygen inhalator and resuscitator (fig. 1).

Use as an Anesthesia Machine

A wide variety of pediatric, obstetric, and surgical operations have been performed with use of the anesthesia machine, without serious complications. The most frequent uses are listed below. 1. For children, prompt, pleasant induction into plane 2 anesthesia with 4 to 20 breaths prior to developing maintenance anesthesia with open drop ether for tonsillectomy and adenoidectomy (4,481 cases) (fig. 2). 2. Obstetric anesthesia for delivery of normal multiparas, for periods of 3 to 12 minutes (394 cases).[3] Episiotomy was done or lacerations were repaired under local anesthesia supplement, as patients emerged from sleep two to five minutes after removal of the mask. In a small percentage it was used for forceps application and in rapid delivery in complicated cases requiring instantaneous delivery because of fetal distress. As an example, forceps deliveries have been effected after 12 to 14 breaths of the mixture. In two instances version and extraction for prolapsed cord were completed three minutes after start of anesthesia. 3. As a supplement to thiopental (Pentothal) sodium for dilatation and curettage in more than 100 cases. 4. In dental surgery for multiple extractions of 2 to 20 teeth in 526 cases.[4] Anesthesia developed to plane 2 surgical stage following 8 to 50 breaths, which correlated with blood stream levels of 9 to 16 mg. of cyclopropane for each 100 cc. of arterial blood. 5. In pediatric orthopedic manipulations of deformities of extremities and in greenstick fractures, 250 cases. 6. With and without muscle relaxants and/or sleep doses of thiopental for intubation, 190 cases. 7. In short five-minute operations such as single and bilateral myringotomy, suture of lacerations, and incision of abscesses or removal of abdominal and perineal packs, 85 cases.

Nonflammable Mixtures of Cyclopropane.—In June, 1954, E. C. Gregg,[5] the professor of physics of Case Institute in Cleveland, considered the relative hazards of explosion associated with the Western Reserve portable anesthetic machine with anesthetic mixtures of cyclopropane and oxygen, as compared to the presently used standard equipment with the same calculated mixtures of the gases. He stated in a personal communication to me:

> The hand unit possesses not more than about one-third of the destructive potential of a standard machine from the viewpoint of primary electrostatic explosion. This ratio becomes very much smaller if one considers an explosion of a standard machine with a leak or an open port such that most of its bottled cyclopropane escaped to the atmosphere and there formed an explosive mixture in the operating room. For a secondary explosion of this kind, assuming a bottle of 378 liters capacity and a room with no ventilation, one

Professor of Anesthesia, School of Medicine, Western Reserve University, and Director of Anesthesia, University Hospitals of Cleveland.

Read before the Section on Anesthesiology at the 106th Annual Meeting of the American Medical Association, New York, June 6, 1957.

would obtain a minimum lower figure of 1 to 240. One could go still further and estimate tertiary effects of knocking over larger bottles of gas in the room and igniting these; however, the major danger here would be from fire rather than explosion, since there would be a slow formation of an explosive mixture. Under any circumstances the portable unit appears very much safer than a standard gas machine.

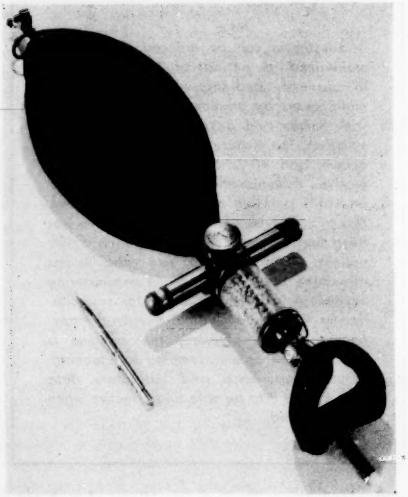


Fig. 1.—The Western Reserve Miniature Anesthesia Machine and Oxygen Resuscitator.

Nevertheless, the use of cyclopropane, ethylene, ether, vinyl ether, ethyl chloride, and most of the recently developed ethers for anesthesia has resulted in potentially explosive mixtures that have in the past been associated too frequently with electrostatic ignition leading to death or serious injury of the patient and with other disasters.

Therefore, in May, 1954, we began to consider means of developing a packaged nonexplosive anesthetic mixture. With C. A. Brown,[6] associate professor of chemistry at Western Reserve University, we reviewed all of the nonflammable mixtures of anesthetic gases developed and the possible additives for cyclopropane-oxygen mixtures. Using the recommendations of Jones and his co-workers [7] and Hickcox [8] concerning the per cent by volume composition of nonexplosive anesthetic mixtures (see table), we have developed nonexplosive mixtures of cyclopropane, oxygen, and helium or nitrogen. We verified the nonexplosibility of our mixtures by placing them in an explosion chamber (fig. 3), and tested for flammability by means of electric spark and flame ignition. The fact that no explosions occurred in our tests with these mixtures confirmed previously published data.

These mixtures have been tested in more than 8,000 short anesthesias in order to determine the safest and most effective mixtures that would preserve the highest concentrations of oxygen, the most rapid induction of anesthesia, and the minimum of undesirable side-effects. To assist us in our determinations of the efficiency of the anesthetic and of safety to the patient, we have in many instances carried out the following studies before and during induction and maintenance of various depths of anesthesia in both children and adults undergoing surgical, obstetric, and dental procedures: electrocardiographic and electroencephalographic studies; spirometry determinations; blood pressure, pulse, and cardiac output measurements; and determination of blood levels of cyclopropane, oxygen, and carbon dioxide. We found that there was no undue depression of vital physiological function below plane 2 of anesthesia in any case.

Having determined what were to be the components of the mixtures, in consultation with George J. Thomas and the testing laboratory of the United States Bureau of Mines, we began the packaging in thumb-sized cylinders of compressed mixtures of cyclopropane and helium and of oxygen and helium in the proportions of nonexplosive potential as defined in the table. Combination of the contents of one cylinder of each type in the machine gives an anesthetic mixture that is nonexplosive. The cylinders are painted different colors for easy rec-

Fig. 2.—Three-liter duck decoy rubber toy bag for inductions of anesthesia in babies and small children.

ognition, and a green cylinder containing the compressed equivalent of 3,400 cc. of oxygen at atmospheric pressure is available for resuscitation and inhalation.

Since the optimal conditions for explosion exist when there are eight parts of oxygen to two parts of cyclopropane, it is obvious that the higher the concentration of cyclopropane, the safer the mixture. This fact has been confirmed by our tests for explosibility of mixtures of cyclopropane, oxygen, and helium in varying proportions. Furthermore, our clinical studies revealed that induction of anesthesia is effected more promptly and smoothly with higher concentrations of cyclopropane. Through a series of clinical tests, we have determined the mixture that produces the most satisfactory clinical results: The green and brown cylinder contains 1,850 cc. of oxygen and 470 cc. of helium; the orange and brown cylinder contains 2,200 cc. of cyclopropane and 1,180 cc. of helium (with recessed metal cap as safety pin index). These cylinders yield 6,000 cc. (30% oxygen, 30% helium, 40% cyclopropane). If the components of this mixture are packaged in two thumb-sized cylinders, with sufficient oxygen and helium in one cylinder and sufficient cyclopropane and helium in the second cylinder to make 6 liters of gas at atmospheric pressure, the mixture remains nonexplosive during the induction of anesthesia in patients of all ages, provided that no pure oxygen is added to the mixture faster than it is taken up by the blood stream.

Per Cent by Volume Composition of Nonexplosive Anesthetic Mixtures of Cyclopropane, Oxygen, and Helium

Cyclopropane	Oxygen	Helium
15	20	65
20	20	60
25	25	50
30	30	40
40	30	30

Safety-Pin Index System.—The perforating pin on the orange-designated side is twice the length and size of that on the green oxygen side, and fits exclusively into the recessed metal convex cap of the anesthetic cylinder; while the perforating pin on the oxygen and helium or oxygen side designated by the green band is of smaller size and perforates exclusively the unrecessed metal cap of the oxygen and helium or oxygen cylinders. This safety device eliminates the possibility of the simultaneous use of two anesthetic cylinders to the exclusion of oxygen in the proportion well above the 20% found at atmospheric pressure.

Laboratory Correlation of Clinical Results.—In this phase of our study we have used the 40% cyclopropane–30% oxygen–30% helium mixture in the anesthetization of 79 test patients of varying ages, weights, and physical conditions undergoing surgical, obstetric, and dental procedures. During these anesthetizations 529 samples were taken from the rebreathing bag of the machine into 20-cc. vacuum tubes, as illustrated in figure 3, and more than 2,000 quantitative and qualitative gas measurements were done by the chemical method described by us in a previous publication. Cyclopropane was absorbed from the mixture in the Haldane-Boothby-Sandiford apparatus (modified by us) by means of sulfuric acid. Carbon dioxide was absorbed from the residue mixture by potassium hydroxide. Oxygen was absorbed from the final residue mixture by potassium pyrogallate. After cyclopropane, water vapor, carbon dioxide, and oxygen were absorbed from the samples in the rebreathing bag, the final residue could be considered to be nitrogen and helium—both inert diluents and nonexplosive buffers.

Statistically useful data are available for 6 minutes of anesthesia for all of these cases; recently we have determined additional information in other cases from 12 to 90 minutes of such administered anesthesia. In these 79 patients, plane 1 or 2 anesthesia was induced after 6 to 12 respirations without exception. At all times during the first six minutes of anesthesia the proportion of oxygen in the mixture in the closed system remained above 20%, and the cyclopropane level gradually diminished from 40 to 20%. Initial oxygen concentrations averaged 29% at the beginning of the anesthetization and 23% at the end, while the level of cyclopropane

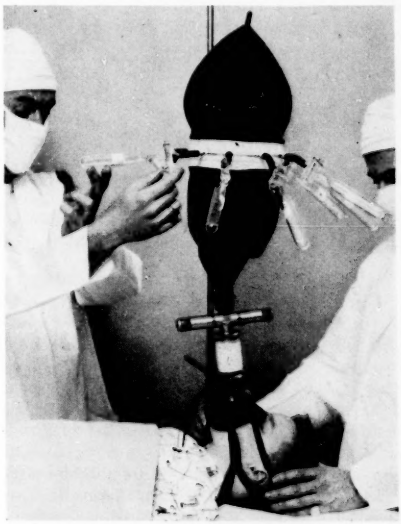


Fig. 3.—The Western Reserve Midget Anesthesia Machine with special circumferential ports with 10 20-cc. sampling vacuum tubes for qualitative and quantitative gas analysis.

in all cases had fallen into the safety range below 25% after six minutes. When a 100-cc. soda lime canister was used with fresh material, the carbon dioxide content of the rebreathing bag remained below 3% after six minutes.

Ninety-six per cent of the samples were outside the spark and flame ignition range; 3% revealed that the mixture had momentarily moved into the flame ignition range; and 1% of the tests revealed a momentary spark ignition range. However, a substantial number of these flammable samples were predictable because pure oxygen had been added to the anesthetic mixture. In the light of our recent experience, a further number could have been made nonflammable through our presently used precaution of weighing the filled cylinders on a microscale. The underfilled cylinders representing by weight an error of plus or minus 3% are discarded. The approximately 1% of unpredictably potentially dangerous samples were probably due to mechanical failure. Already progress has been made in eliminating this hazard entirely.

When one considers that an anesthetic explosion presently occurs no more frequently than 1 in 75,000 with presently used safeguards, the reduction of anesthetic explosion potential by at least another hundredfold represents a substantial progress in permitting the return of safer and more predictable instantaneous anesthesia to the emergency outpatient room, the properly equipped dental office, the accident admitting division, the x-ray room, and, of greater importance, the military bases and warships at sea presently denied this essential service.

Use as an Inhalator

The first objective in the design of the equipment has been the adaptation of portable, readily accessible oxygen for resuscitation and for use in a therapeutic closed inhaler and escape gas mask. This has been accomplished by engineering design of a compact 2-lb. unit easy to operate and efficient in its provision of oxygen in atmosphere, stabilizing after several inhalations at 60% to 80%; of equal importance is its absorption of carbon dioxide with a closed to and fro canister system offering the minimum of resistance. The latter has been accomplished for as long as necessary with canisters of 100 cc. for 15 minutes, 200 cc. for 30 minutes, or 350 cc. for up to two hours.

The oxygen is packaged under pressure of 4,000 lb. per square inch in 10-cc. metallic containers about the size of the thumb, capable of holding about one free volume gallon (3,400 cc.) or sufficient oxygen for an adult at rest for 10 minutes per cylinder or the oxygen requirements when walking at a rate of 3 miles per hour for 200 yd. By a simple wrist turn of the side-arm container of the cylinder, the compressed gas is readily released through directional ports into a 6½-liter rebreathing bag by a perforating pin mechanism.

Method of Operation.—Press the mask firmly on face, with special attention to leak-proof fitting around bridge of nose. A red band will be noted around the snap assembly unit just above the mask. When the mask is pressed firmly to the face, the release valve will open. The red band will then disappear, indicating an unobstructed oxygen flow into the mask.

Use as a Resuscitator

Oxygen in the Physician's Satchel.—Neither the 10 phamaceuticals in the physician's satchel of a quarter century ago nor the 10 wonder drugs in his satchel in 1957 contain the most essential element for saving life, namely, oxygen. Yet, promptly and properly administered by general practitioners, pediatricians, dentists, or by members of the surgical specialties, 100% oxygen in the alveolar reservoirs (lungs) is the agent most needed and most effective in maintaining life.

Hypoxia is usually the precursor of death in disease, fatal accidents, under anesthesia, in infant resuscitation, and in fire and military disasters, yet a very small percentage of physicians, nurses, or rescue personnel could initiate or maintain a clear airway in the unconscious obstructed patient. Fewer still could develop the optimal respiratory cycle through artificial respiration effecting an adequate tidal volume or proper positive atmospheric and negative pressures to deliver oxygen and eliminate carbon dioxide.[6]

In emergencies associated with hypoxia the modern physician relies too greatly upon pharmacological injections. This is particularly serious when the needed treatment is oxygen, an unobstructed airway, elimination of carbon dioxide, and a return of blood to the heart sufficient to yield the next essential beat. The use of autotransfusion by elevating the legs will supply the central circulation in a few seconds with 600 cc. of well-matched blood which can be maintained by such devices as ace bandages or elastic stockings.

Paluel Flagg, in the August, 1953, issue of *General Practitioner*, strongly stated the obligation of the physician to reduce the death toll and brain damage due to lack of oxygen, which he stated to be twice that due to automobile accidents. While millions are being spent annually to reduce the automobile accident death rate, why is the situation in relation to oxygen lack allowed to remain the same? There are two basic reasons:

1. Lack of proper education for both physician and lay rescue squads in recognizing the need for and in performing resuscitation. Even when the necessity is recognized, the limitations of the generally used manual method of artificial respiration are not fully understood. As the need for resuscitation increases, often less than 150 cc. of air can be forced into the lungs by this method. This roughly corresponds to the dead space in the respiratory system, which does not come in contact with the alveolar membranes through which oxygen passes into the blood stream.

2. Lack of proper resuscitation apparatus that is convenient for use by all types of rescue personnel. The apparatus should be (*a*) readily available and easy to operate; (*b*) easily portable so that patients do not have to be moved before assistance is given; (*c*) safe in operation, i. e., designed to prevent any damage to the patient during resuscitation even by inexperienced laymen; (*d*) simple to operate, necessitating only limited training with the equipment.

Attempts at proper education are constantly being made by medical schools, civil defense units, police and fire departments, Red Cross units, and other groups interested in this problem. Emphasis is placed on immediate treatment to free the patient's airway of obstruction and to get oxygen to the lungs as soon as possible to prevent irreversible brain damage. Various methods are usually presented, from the simplest to the use of complex machines. If the patient receives adequate oxygen therapy before his circulation fails, it does not matter how it is given. Probably the most effective simple method is the use of the Safar double airway.

The Western Reserve University device meets these requirements. This machine can provide oxygen conveniently, both as inhalator and as resuscitator, under many conditions: 1. For the general practitioner. This device will readily fit into his bag. 2. For the rescue squad. It can fit into a man's pocket. 3. For the home cardiac, asthmatic, or anemic patient in temporary distress. It is instantaneously available at the bedside.

Technique for Use as a Resuscitator.—When this device is to be used as a resuscitator, it is important that the patient be lying on his back with feet higher than his head, in order to (1) initiate greater blood return to heart to aid maintenance of blood pressure; (2) help clear the lungs and bronchi of any foreign matter. Special attention should be given to clearing the throat of any obstruction before the unit is applied to the patient. This may be accomplished under direct vision, by use of suction apparatus or mouth suction through rubber tube or soda straws. An unobstructed airway to the lungs is essential and can be insured by means of the Guedel airway (rubber or plastic) of proper size (adult, child, or infant) (fig. 4). If not available, lift the lower jaw forward and upward by extending head on neck, supporting the angles of the jaw. Hold chin up. In cases of drowning a suction is useful, but oxygen under intermittent pressure should have priority. After a clear airway is established, the machine is placed on victim's face, with mask fitting snugly, and headstrap is snugly applied. With the last two fingers of the left hand of operator the patient's jaw is supported. The thumb, index, and middle fingers keep pressure on face mask. The right hand compresses and releases bag rhythmically 12 to 15 times per minute, with sufficient pressure to force oxygen into victim's lungs. The amount of pressure necessary can be determined by observing

Fig. 4.—Proper application of specially equipped Western Reserve Resuscitator to patient's face in respiratory arrest. Note this machine is equipped with two additional central axial bodies, maintaining a combined loaded capacity of 6 oxygen cylinders or 20 free volume liters of 100% oxygen. If leaks are avoided this is sufficient oxygen for more than 30 minutes of resuscitation.

chest expansion and deflation during respiratory cycle. It is not necessary to press the bag too firmly. There is a pressure-limiting safety valve, set at +20 mm. Hg to prevent overinflation of the patient's lungs.

The operator should make sure the bag is inflated at all times, i. e., as soon as the bag is half empty, add another cylinder. This enables the operator to exert more efficient positive pressure on the bag, as well as keeping down the carbon dioxide volume percentage. Removal of the machine should occur only when the victim shows signs of recovery.

If the machine is equipped with the 100-cc. canister of soda lime, it may be used for approximately 20 minutes without a dangerous amount of carbon dioxide building up. However, if fresh soda lime is not then available, the machine should be removed from the victim's face and the bag should be emptied completely and refilled with pure oxygen; this procedure should be repeated each five minutes.

The physician may recommend this machine to his patients for self-administration as an inhalator, following the same rules of safe oxygen therapy as previously outlined.

Care of Western Reserve Machine

Of special significance in tuberculosis and respiratory infection, the Western Reserve machine may be disassembled completely and washed in lukewarm soapy water, with use of a toothbrush to scrub the metal parts. All parts should be rinsed thoroughly and the bag hung up to dry with loop provided. It is recommended that this be done periodically, to prolong the life of the unit. After repeated use of the Western Reserve unit the soda lime will turn whitish in color. The soda lime must then be changed and reactivated by removing the canister and refilling with a fresh package of soda lime; care should be taken to blow out dust. (The used soda lime may also be activated by placing it in a dish and putting it in a 250 F oven for 10 to 15 minutes, or until the lime turns to its natural color —pink.)

Carbon Dioxide Studies

Our carbon dioxide studies have revealed that the use of a 200-cc. soda lime canister provides a removal of carbon dioxide for periods of one hour in adults. Carbon dioxide is kept below 3 vol. % in this closed ventilation system of artificial respiration. Therefore, this canister should always be used for periods longer than 5 minutes, whether the equipment is being used as an inhalator, resuscitator, or anesthesia machine.

At the time of writing, the machine has been tested thoroughly for a period of three years with a research staff of six medical students, three university professors of physics, chemistry, and anesthesia, and three design engineers; its use can be documented in more than 8,000 short anesthetic procedures and operations in our hospitals and more than 2,000 additional cases from physician research consultants in other universities and hospitals in the United States, Canada, Great Britain, Europe, South America, and Japan. This machine has been used successfully in 2 cases in which it was the sole source of oxygen in treatment of cardiac standstill and in an additional 28 reported cases of serious respiratory arrest during anesthesia or as a result of traffic accidents.

Summary and Conclusions

During the past five years a new midget portable model anesthesia machine, oxygen inhalator, and resuscitator has been developed. To date more than 10,000 patients have been anesthetized with this machine, which utilizes nonexplosive mixtures of cyclopropane, helium, and oxygen, without major complications in the previously designated categories. In two cases patients with diagnosed cardiac standstill have been restored with the sole source of the oxygen used in the resuscitation coming from the thumb-sized cylinders. Babies and children responded favorably psychologically to the toy-sized and colorfully attractive machine and went promptly to sleep without struggling or excitement after the 4th to 12th breath. We have also had good results in obstetric patients with accelerated terminal labor, ambulatory dental patients, and patients requiring emergency anesthesia.

2065 Adelbert Rd.

References

1. Lelievre, R. E., and Eickhoff, T. C.: Development of Non-explosive Helium-Oxygen-Cyclopropane Anesthetic Mixture for Use in Western Reserve Portable Anesthesia Machine, Thesis, Western Reserve University School of Medicine.

2. Hingson, R. A.: New Portable Anesthetic Gas Machine and Resuscitator: Preliminary Report, J. A. M. A. **156**:604-606 (Oct. 9) 1954.

3. Hingson, R. A., and Hellman, L. M.: Anesthesia for Obstetrics: Labor, Delivery, Infant Care, Philadelphia, J. B. Lippincott Company, 1956. Tricomi, V.; Bauer, D. P.; and Hellman, L. M.: Applications of the Reserve Midget Machine in Obstetrical Anesthesia: Preliminary Report, Am. J. Obst. & Gynec. **72**:326-331 (Aug.) 1956.

4. Hingson, R. A., and Corcoran, J. W.: A New Portable Resuscitator and Anesthetic Gas Machine, Dental Digest **61**:303 (July) 1955.

5. Gregg, E. C.: Personal communication to the author.

6. Brown, C. A., and Weiss, M.: Sampling and Analysis of Cyclopropane Anesthesia Mixtures, to be published.

7. Jones, G. W.; Kennedy, R. E.; and Thomas, G. J.: Explosive Properties of Cyclopropane: Prevention of Explosions by Dilution with Inert Gases, R. I. 3511 (1940) and 653 (1943), United States Department of Interior, Bureau of Mines.

8. Hickcox, C. B., in Anesthesiology by Forty American Authors, edited by D. E. Hale, Philadelphia, F. A. Davis Company, 1955, pp. 706-724.

9. Dill, D. B.: Introduction, Symposium on Mouth-to-Mouth Resuscitation (Expired Air Inflation): Report to Council on Medical Physics, J. A. M. A. **167**:317-319 (May 17) 1958. Gordon, A. S., and others: Mouth-to-Mouth Versus Manual Artificial Respiration for Children and Adults, ibid. **167**:320-328 (May 17) 1958. Elam, J. O.; Greene, D. G.; and Clements, J. A.: Oxygen and Carbon Dioxide Exchange and Energy Cost of Expired Air Resuscitation, ibid. **167**:328-334 (May 17) 1958. Safar, P.: Ventilatory Efficacy of Mouth-to-Mouth Artificial Respiration, ibid. **167**:335-341 (May 17) 1958.

OXYGEN THERAPY—AN UNSUSPECTED SOURCE OF HOSPITAL INFECTIONS?

C. R. Macpherson, M.D., Columbus, Ohio

A humidifying device typical of the apparatus generally used in connection with oxygen therapy was studied bacteriologically as a possible source of contaminant organisms in the hospital. Samples of water taken from the reservoirs of the humidifier revealed a marked degree of contamination in a large percentage of cases. Although most of the bacteria found were nonpathogenic, a few were dangerous, and the extent of contamination was greater than had been anticipated. As a result, a systematic procedure for the care of humidying units in oxygen therapy has been adopted. The water to be used must be sterile, and when the level in the reservoir falls the residue must be discarded and replaced, not merely replenished. Certain policies regarding sterilization should be followed, and after each period of use the glass reservoir must be cleaned and inspected before the unit is used again or stored.

Oxygen, as an essential part of modern therapy, has been extensively investigated, but bacteriological study of the apparatus used in this form of therapy seems to have been neglected. A review of the available literature on oxygen therapy in general and on humidification apparatus in particular has failed to provide any information on this aspect other than general statements, such as "The entire unit can be dismantled and sterilized in an autoclave." [1] Even where such statements are made, no reason is given for this use of the autoclave, other than the general, obvious, and unspoken one that all therapeutic apparatus should be clean.

This investigation was accordingly undertaken to determine three things: 1. In the efficient, well-run oxygen therapy unit of a modern teaching hospital, is contamination of the apparatus a real factor or only an imaginary hazard? 2. If contamination does exist, does it involve pathogenic organisms or only harmless saprophytes? 3. If contamination by pathogenic organisms is a real hazard, what modifications in procedure would be necessary to ensure sterile, or near sterile, operation?

Materials and Methods

Since no investigations had been reported, it was necessary to improvise and test methods of sampling, as well as to decide which pieces of apparatus, and how many parts of each piece, required investigation.

The figure shows a humidifier (Oxifier) of the type which comprised about 85% of the humidifying apparatus in the hospital at the time this investigation was begun. The several other types of apparatus in use need not be considered further, since they presented similar problems in sampling and the findings were essentially the same as those reported for this type.

The attachment and pressure-release valves (figure, *A* and *B*) were sampled with a swab moistened in sterile saline solution. Tubes of thioglycollate glucose broth were then inoculated and incubated at 37 C for four days. The water reservoirs were tested by removing 5 ml. of water with a sterile pipet. This was then either cultured in a flask containing thioglycollate glucose broth or else used for plate counts.

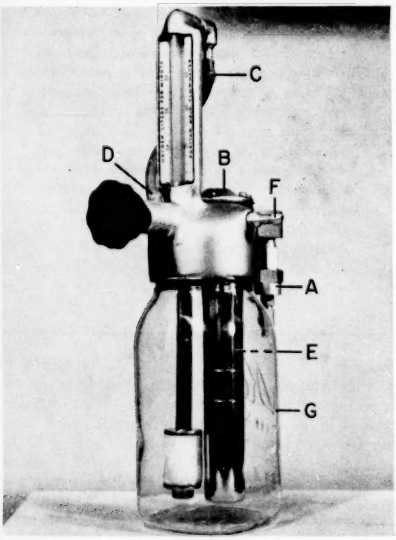
The oxygen coming into and leaving the humidifier and the outlet ducts in the humidifier could not be tested by these techniques. The system devised was based on the use of sterile tubing to bubble oxygen through a culture medium. Standard Bunsen tubing was cut into 10-in. lengths, placed in individual paper wrappers which were stapled shut, and put into an autoclave at 15 lb. of pressure for 20 minutes. This ensured a supply of sterile tubing which was easy to prepare and store. The medium used throughout was thioglycollate glucose broth. Fifty-milliliter amounts were placed in 6-oz., round, screw-capped bottles and put into the autoclave. When the incoming oxygen was being tested, the sterile tubing was attached to the connection at the upper end of the flowmeter (figure, *C*). The other end of the sterile tubing was placed just below the surface of the medium in the bottle and the oxygen run at exactly 5 liters per minute for exactly four minutes, thus ensuring each time that a comparable sample of 20 liters of oxygen was tested. There was no constant or reproducible difference in results, whether the oxygen ran at 2, 4, 5, or 6.6 liters per minute. However, the slower rates made sampling very tedious, and faster rates resulted in rather excessive splashing, so that 5 liters for four minutes was chosen as the best compromise and adhered to throughout.

Chief, Division of Bacteriology, Department of Pathology, Ohio State University.

958
167

To sample the condition of the outlet ducts in the humidifier, without interference from organisms carried over from the water reservoir, duplicate reservoirs were filled with water to the usual level, paper covers were attached, and the reservoirs then put into the autoclave. These sterile reservoirs then replaced the regular reservoir, sterile tubing was substituted for the outlet connection, and the sample was taken as described above.

The patient delivery tubing was in 6-to-9-ft. lengths. It was sampled before and after cleaning by running 10 ml. of the sterile thioglycollate medium into one end, with the other end pinched closed. With both ends pinched closed, the broth was run from one end to the other several times



Humidifying apparatus in general use at time of investigation: *A*, attachment to wall outlet; *B*, pressure-release valve; *C*, flowmeter outlet tubing, upper end; *D*, flowmeter outlet tubing, lower end; *E*, tube to outlet with baffle-plate at top; *F*, patient outlet; *G*, glass reservoir.

by elevating alternate ends and was then decanted into a sterile test tube for incubation at 37 C for four days.

Results

Testing of the oxygen from the upper flowmeter outlet and from the wall-connection itself showed uniformly sterile cultures, with the exception of an occasional organism which was almost certainly the result of accidental contamination, since completely aseptic sampling technique is virtually impossible. Swabbing of the pressure-release valve gave equally negative results.

As shown in table 1, the samples of water taken from the reservoirs revealed a marked degree of contamination in a large percentage of cases. The degree of contamination of the outlet ducts was also high, though not so marked as that of the reservoir water, and there was a lack of correlation in the number of organisms recovered from the two sources in individual pieces of apparatus.

The water used in the reservoir bottles was distilled, though not sterile, and it was difficult to understand why there was such a variation in the number of organisms present as well as such a high general level. Further investigation showed that there were four sources of contamination of this water: (1) the carboys in which the water was delivered to the hospital, (2) the siphon (rubber and glass tubing) used to withdraw water from these carboys, (3) the bottle used to take water around to the rooms in order to replenish the reservoirs of the units in operation, and (4) the habit of replenishing the reservoir bottles periodically as long as the unit was in operation for the same patient without first emptying out the remaining water.

It was found that there was no regular, automatic cleaning of the carboys at the source of the distilled water supply. As a result, distilled water only a day old was found in some cases to have a count of over 2,000 organisms per milliliter. A simultaneous check of a commercial distilled water advertised as being in "sterilized containers" showed that six carboys had a count of from 3 to 1,500 organisms per milliliter.

Contamination of the water was easily eliminated by switching to the use of commercial, sterile, distilled water. Cleaning the outlet ducts of the humidifiers (figure, *E* and *F*) was more of a problem. Several methods were tried. Originally, the ducts were rinsed through with disinfectant, followed by detergent and then by tap water. Next, the detergent was used before the disinfectant, followed by tap water and distilled water rinses. Another method employed was to hook the unit over the edge of a container full of a cationic detergent in such a way that the outlet ducts were below the surface while the release valve and the flowmeter remained dry. The unit was allowed to soak overnight and was then thoroughly rinsed. Finally, when these methods had been proved to be unsatisfactory, the unit was disassembled as far as possible and cleaned with a swab soaked in detergent, rinsed, and reassembled.

All these procedures failed to ensure even a reasonable degree of cleanliness (table 1), although the percentage of grossly contaminated reservoirs was considerably reduced. It was obvious that use of the autoclave would be the method of choice, but it was hoped to avoid this, since both the pressure-release valve and the flowmeter would be

damaged. However, a later model of the same humidifier, the Oxijet, is made from stainless steel, including the release valve, and appears to be suitable for autoclave sterilization.

With regard to the types of organism recovered from the humidifying apparatus in this survey (table 2), it will be noticed that the majority are Enterobacteriaceae of a type falling under the general designation of "water bacilli," that is, of a type commonly recovered from water supplies and usually nonpathogenic for man. However, a variety of organisms was found, possibly the most alarming of which was a gas-producing Clostridium, finally classified as an atypical Cl. perfringens (Cl. welchii). Fortunately, the apparatus from which this was isolated was not in use. It was on a surgery floor, but there is no record that any patient in that room suffered from gas gangrene. The outlet tubings were, in general, clean, only light growth of Staphylococcus pyogenes var. albus or of diphtheroids being recovered from the washings.

TABLE 1.—*Cultures of Humidifier Reservoirs and Outlets*

	Reservoirs							Outlets						
		Contamination							Contamination					
		Gross*		Slight†		Total			Gross		Slight		Total	
	No. of Samples	No.	%	No.	%	No.	%	No. of Samples	No.	%	No.	%	No.	%
Original sampling	46	27	59	14	30	41	89	37	5	14	12	32	17	46
Sampling after revision of cleaning technique	15	3	20	10	67	13	87	15	2	13	10	67	12	75

* Gross contamination determined by visible growth in less than 18 hours.
† Slight contamination determined by visible growth in more than 18 hours.

Comment

The results obtained were unexpected. Since the equipment was not routinely sterilized, some contamination was inevitable, but the extent was greater than had been anticipated. Secondly, the oxygen therapy service, to an impartial observer, appeared to compare very favorably with similar services encountered in other hospitals, as regards organization, cleanliness, and concern to improve methods and service. This inevitably raises the question as to what would be found on similar investigation in other establishments. It appears unlikely that conditions are much better elsewhere, from discussions held with people directly concerned with such matters.

With regard to the third question asked at the beginning of this article, before attempting to provide an improved service one must bear in mind several factors. In the first place, the difficulty of obtaining suitably trained personnel being what it is, the system should be as simple and reproducible as possible, to avoid undue expenditure of time by highly trained personnel. Secondly, it should not be prohibitively expensive. Thirdly, a careful balance needs to be struck between what is practicable and what is actually required. For example, aseptic technique throughout would not only be prohibitive in terms of both time and money, but it would be quite unjustifiable, since the air of the room itself is always heavily contaminated. However, it is justifiable to aim at a high degree of cleanliness, since the organisms present in the stream of oxygen are being introduced, under conditions favorable for the establishment of infection, into patients whose pulmonary mechanics render them particularly susceptible to infection. Although no accurate figures exist as to the frequency of patient infection resulting from contaminated oxygen therapy apparatus, it was unanimously agreed by all concerned that this final proof was not necessary. The weight of circumstantial evidence was considered sufficient to justify an immediate change in technique.

For these reasons, the following points were adopted in the Ohio State University Health Center: 1. All water used in humidifying apparatus must be sterile. 2. No apparatus can be in service for a patient for longer than one week. 3. The water in the humidifier must be discarded and replaced when the level falls due to use. The humidifier cannot be replenished without first emptying it. 4. Each time service is discontinued, or after a period of one week of service, the glass reservoir

TABLE 2.—*Analysis of Organisms Recovered from Reservoirs and Outlets of Humidifier*

Type of Organism	Times Found No.*	% of Total No. of Samples
Achromobacter and Alcaligines fæcalis	33	29
Pigment-producing bacilli (various types)	14	12.5
Staphylococcus pyogenes var. aureus (coagulase positive)	12	10.5
Diptheroids	3	2.7
Clostridium perfringens (Cl. welchii)	1	0.9
Bacillus subtilis	3	2.7
Staphylococcus pyogenes var. albus	4	3.5
Pseudomonas aeruginosa	6	5.3
Yeasts and fungi (nonpathogenic)	3	2.7
Streptococcus viridans	1	0.9
Enterococci	1	0.9
Paracolon bacilli	1	0.9
Escherichia	1	0.9
Klebsiella	1	0.9
Nonpathogenic mycobacterium	2	1.8
Sterile samples	29	26

* More than one organism was recovered from single sample on occasion.

must be cleaned with an antiseptic and a detergent and the rubber washer must be carefully inspected. If any cracks are found, the washer is to be replaced. 5. As soon as suitable apparatus is available, the metal top of the humidifier will be put in the autoclave between patients, or after one week, as in point 3. 6. All stored apparatus must be dry. The glass reservoirs must be inverted or covered. 7. Wherever possible, disposable tubing should be used, rather than tubing requiring cleaning. 8. Bacteriological spot checks are to be run at regular intervals.

With reference to the last entry in table 2, the recovery of nonpathogenic mycobacteria in two cases, it should perhaps be emphasized that these were the only two units tested for the presence of Myco. tuberculosis and that they came from another hospital which specializes in the treatment of tuberculosis.

Summary

Systematic investigation of apparatus used in the oxygen therapy section of a large teaching hospital revealed gross contamination in a high percentage. Three main sources of infection were believed to be responsible: (1) contamination of distilled water before it reached the hospital, (2) difficulty in obtaining adequate cleansing of apparatus, and (3) lack of any standard technique specifically designed to prevent contamination.

In view of the lack of previous studies, it is thought that a similar situation may exist in other hospitals. Specific recommendations are made to eliminate the major sources of contamination and include sterilization of the apparatus concerned.

Miss Judith Hiller supplied technical assistance.

References

1. Denton, R., and Smith, R. M.: Portable Humidifying Unit: II. Large-Capacity Metal Nebulizer, A. M. A. Am. J. Dis. Child. **82:**433-438 (Oct.) 1951.

A NEW APPARATUS FOR ARTIFICIAL RESPIRATION

Jacques Trémolières, ESBB, Stains (Seine) France

Advances in the pathological physiology of respiration have made possible corresponding improvements in apparatus for artificial respiration. Patients with poliomyelitis often need artificial respiration given by such means, but patients anesthetized for surgery, especially under the influence of depressant or relaxant drugs, often also need respiratory assistance in order to maintain normal relations of oxygen to carbon dioxide in the blood. In either type of patient, if the diaphragm or the intercostal or other muscles of respiration are seriously involved, some sort of respirator is a necessity.

The ideal respirator should incorporate some sort of control by the patient, so that frequency and depth will be instantly adjusted if the patient begins to breathe spontaneously. If no provision is made for this possibility, patient and machine are likely to work against each other, and a distressing phenomenon called "bucking the respirator" results. If the patient initiates his own breathing, the automatic cycling of the respirator should stop, so as to allow him to do his own breathing without interference. It is further desirable that the respirator should act not only as insufflator during inspiration (positive pressure phase) but also as aspirator during expiration (negative pressure phase).

The ideal respirator should incorporate some sort of control by the patient, so that frequency and depth will be instantly adjusted if the patient begins to breathe spontaneously. If the patient initiates his own breathing, the automatic cycling of the respirator should stop, so as to allow him to do his own breathing without interference. The Pesty positive-negative pressure respirator makes it possible to give artificial respiration by a process of active inflation and deflation at amplitudes and frequencies determined by the operator. No source of electricity is needed, since the required energy is supplied by the compressed air. Mixture of anesthetic gases can be administered in place of compressed air.

This second phase is important, as has been pointed out by Maloney and associates [1]:

In the group of patients who had some degree of respiratory and/or circulatory inadequacy . . . devices that employ positive pressure only were found to cause a fall in blood

pressure and cardiac output, sometimes of sufficient magnitude to threaten the life of the patient. On the other hand, the use of a machine employing a negative pressure phase during expiration avoided this circulatory depression, and permitted the patient to maintain blood pressure and cardiac output at more normal levels.

This opinion is shared by Hubay and his coworkers [2]:

In the closed chest, intermittent positive-negative pressure respiration increases venous return significantly over that measured during positive-atmospheric pressure respiration. The use of a negative pressure phase, between positive pressure lung inflations in the closed chest, is physiological since the mechanisms of increased venous return correspond to those observed with spontaneous respiration.

Positive pressure lung inflation in the closed chest decreases venous return by decreasing the pressure-gradient from extrathoracic to thoracic veins.

These considerations show that the tank respirator, so far from being the only useful means of artificial respiration, can actually be singularly harmful. This has been stated by Bower and others [3]:

For some time I have been dissatisfied with the performance and action of the standard tank-respirator. In many severe cases it did not permit adequate exchange of oxygen and carbon dioxide during the respiratory cycle, and the pattern of breathing to which the patient was forced to conform did not simulate a normal pattern. Furthermore, in many instances we noted that inability to cough or swallow, laryngospasm, and other factors augmented this inadequate gaseous exchange, preventing the patient from ridding the larynx, trachea, and bronchial tree of excessive amounts of secretion, thus causing additional trouble or death.

It is with these considerations in mind that I present a description of a volume-regulated respirator. Developed on the basis of two years of experiments with dogs, it has been tested in a one-year clinical trial with human subjects.

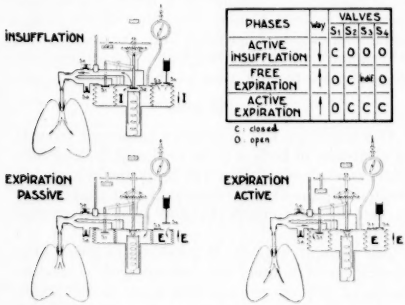


Fig. 1.—Positive-negative respirator, showing insufflation and expiration.

Description

The Pesty positive-negative pressure respirator makes it possible to give artificial respiration by a process of active inflation and deflation at amplitudes and frequencies determined by the operator. The air-passages within the apparatus are so arranged as to send the air expired by the patient through a spirometer, which measures the volumes concerned and so reveals leaks anywhere in the

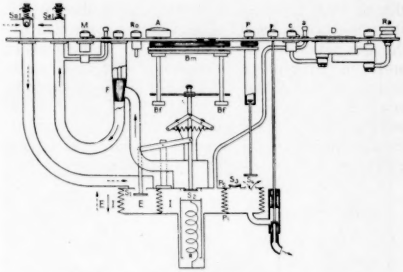


Fig. 2.—Diagram of respirator. *Bm*, movable guard; *A*, regulation screw of movable guard; *Bf*, fixed guard; *F*, braking device on inspiratory circuit; *P*, regulation screw for pause; *p*, device for removing condensed water; *c*, connector cock; *a*, rebreathing bag joint (for manual action); *D*, flow meter; *Ra*, gas in; and *Ro*, regulation cock for aspiration.

system. Without affecting the adjustment of amplitude and frequency, it is also possible to vary the relative duration of inspiratory and expiratory phases of respiration. No source of electricity is needed, since the required energy is supplied by the compressed air.

The respirator is composed of two concentric or coaxial bellows (fig. 1 and 2, *I* and *E*). These have one wall and two plates in common. The lower plate (*Pi*) is fixed; the other plate (*Ps*) is moveable. The air or gas from the source-tank for inspiration is delivered into the central bellows (*I*). As this bellows expands, it pushes the movable common plate upward. This carries along the outer bellows (*E*), generating a negative pressure and causing the deflation of the patient's lungs. The upward movement of the upper plate (*Ps*) is caused by the compressed air; its return movement is caused by a spring (*R*). The respective volumes of the two bellows are such as to make sure that the outer bellows causes an adequate expiratory movement in the patient.

Valves *S1* and *S2* are so connected with the apparatus that they must close or open in opposition. When *S1* is open, *S2* is shut. When the upper plate rises during the entrance of the compressed air, *S1* opens to permit the patient's expiratory air to be drawn into the outer bellows. When the upper plate returns, drawn by the spring, *S1* closes, *S2* opens, and the air from the inner bellows passes out to insufflate the patient's lungs (fig. 1*A*). The supply of air from the tank is continuous, but the move-

ments of valve *S2* determine the direction of movement of the bellows and are thus responsible for the cycling of the apparatus.

During that part of the cycle when the plate descends in response to the force of the spring and air is passing from the inner bellows to the patient, the air from the outer bellows is being discharged from the exit valve *S3*. This valve is controlled by the difference between the pressure in bellows *E* and the atmospheric pressure. When the plate reascends and bellows *E* and *I* are increasing in volume, the pressure in bellows *E* is negative or subatmospheric. This causes valve *S3* to close. At the beginning of the ascent, the valve *S1* opens suddenly and so establishes communication be-

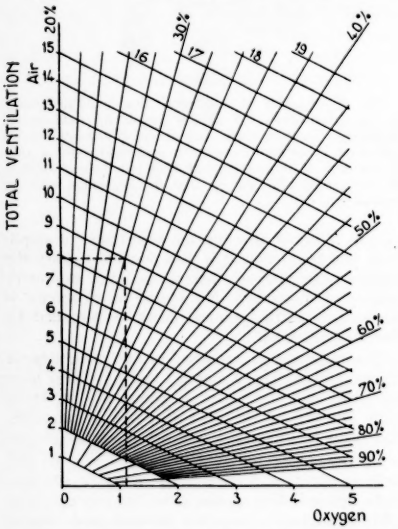


Fig. 3.—Air-oxygen graph for determining rate of ventilation. Abscissa shows flow of oxygen in liters per minute; ordinate shows flow of air in liters per minute; divergent lines show oxygen concentration.

tween bellows *E* and the lungs, which are full of air under positive pressure. Valve *S3* offers a very low resistance to the discharge of the expired air and continues to permit its escape as long as the pressure in bellows *E* exceeds atmospheric pressure.

Having permitted a certain amount of expired air to escape, valve *S3* closes. The plate continues to ascend, the pressure in bellows *E* becomes increasingly negative, and the lungs of the patient are actively deflated. It is logical to want to adjust, and indeed necessary to limit, the negative pressure, and that is the function of valve *S4* (fig. 1*B*).

Valve *S4* is suspended above bellows *E* in such a way that the distance between the valve and the bellows in its low position is adjustable. As a result, when the bellows are filling and the plate is moving up, valve *S4* is opened at a certain stage. The exact instant at which *S4* is to open is determined by its setting, and the expiratory or aspirating effect of bellows *E* begins only after valve *S4* is closed. By thus determining the extent of the expiratory action of the bellows, valve *S4* makes it possible to adjust the amplitude and duration of the expiratory phase of respiration (fig. 1*C*).

Further adaptation to the patient's needs is provided for by the existence of a period of inactivity between the active inflation and deflation phases. During this period there is time for the intrapulmonary pressure to approximate atmospheric pressure.

Two other valves, *Sa* and *Se*, will be found on the expiratory and inspiratory circuits respectively. They are safety valves provided with tared springs which prevent the pressures in the lungs from exceeding the limits of safety in either the positive or the negative direction.

Operation

It was noted above that the direction of movement of the bellows is decided by the setting of valve *S2*. Valves *S1* and *S2* are connected by a lever which is governed by a bascule system in such a way that only two positions of equilibrium are possible. The shift from one position to the other is brought about by the striking or impinging of the bascule system against two guards. One guard (*Bf*) is fixed; the other (*Bm*) can be set at various positions. The distance between the two guards determines the amplitude and, consequently, the tidal volume. The amplitude is measured in millimeters of bellows motion. The valve *S4*, set along a millimeter scale, determines the duration of the pause, and the relation, R=pause÷expiratory time, gives the relative duration of the pause.

Application

It is necessary first to decide whether air, oxygen, or a mixture of both is to be used and to determine what rate of ventilation (in liters per minute) is desired. Figure 3 is a nomogram that enables one to set the flow-meters to give a predetermined ventilation rate.

For example, suppose it is desired to give a total ventilation of 9 liters per minute with a mixture having a 30% oxygen concentration. In the graph, one seeks the intersection point of ventilation line 9 with the concentration line 30%. The abscissa of this point is 1.1 (flow of oxygen in liters per minute); the ordinate is 7.9 (flow of air in liters per minute).

Figure 4 is a nomogram that enables one to determine what frequency and amplitude of cycling should be used. The frequency is important, be-

cause too fast a rate of cycling decreases the efficiency of alveolar ventilation, while too slow a rate may increase the tidal volume beyond the pulmonary capacity of the patient. In this graph, the abscissa represents ventilation; the ordinate represents rate. The divergent slanted lines show the resultant tidal volume and amplitude value. A scale at the bottom, parallel to the axis of the abscissa, gives the insufflation speed.

For example, suppose a frequency of 18 respirations per minute and an amplitude of 9 mm. is desired. Two heavy lines in the diagram represent this case. They intersect at a point lying on the slanting line which is marked 500 ml. or 0.5 liter, the proper tidal volume. This figure is seen to correspond to an amplitude of 16.5 mm. The additional scale at the bottom, parallel to the axis of the abscissa, shows that a ventilation rate of 9 liters per minute corresponds to an insufflation speed of 2. These nomograms were determined by spirographic measurements and correspond to a respiratory cycle in which the deflation time is double the inflation time.

Conclusions

This positive and negative pressure respirator [4] (fig. 5) with variable pause has been used successfully in various prolonged respiratory inadequacies such as poliomyelitis, polyneuritis, polyradiculoneuritis, myasthenia, toxic coma, and tetanus.[5]

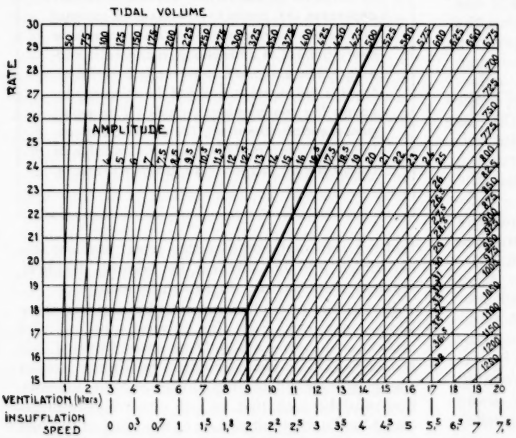


Fig. 4.—Nomogram for determining frequency and amplitude of cycling.

Mixtures of anesthetic gases can be administered in place of compressed air. Huguenard,[6] in particular, used it in 45 cases of major gastrointestinal surgery with cardiopulmonary inadequacy.

The versatility of the apparatus is such as to permit control of (*a*) ventilation per minute, (*b*) tidal volume, (*c*) insufflation speed, (*d*) expiratory pause, (*e*) ventilation rate, and (*f*) positive and

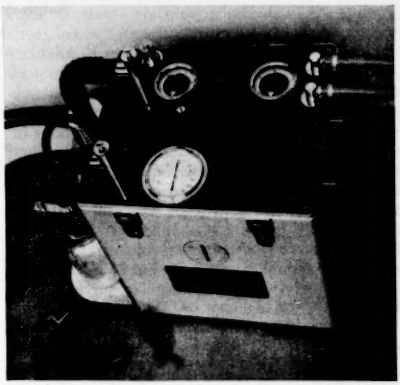


Fig. 5.—Positive-negative pressure respirator.

negative pressure values. When it is used during surgery, the arterial pulse and pressure are stable, bleeding is diminished (capillary bleeding and vasoplegia caused by hypocapnia), and the venous pressure is likewise diminished. The necessary doses of narcotics are less with use of this respirator. These advantages are attributable to the fact that the apparatus is so precisely adaptable to the patient's needs.

46, Av. P.-V.—Couturier, 46, Stains (Seine) France.

Figures 1 and 5 (with slight alterations) are reproduced with permission from *Dessinateurs et Techniciens* (no. 52, pp. 47-52, Jan., 1958).

References

1. Maloney, J. V., Jr., and others: Importance of Negative Pressure Phase in Mechanical Respirators, J. A. M. A. **152**:212-216 (May 16) 1953.

2. Hubay, C. A., and others: Circulatory Dynamics of Venous Return During Positive-Negative Pressure Respiration, Anesthesiology **15**:445-461 (Sept.) 1954.

3. Bower, A. G., and others: Concept of Poliomyelitis Based on Observations and Treatment of 6,000 Cases in Four-Year Period, Northwest Med. **49**:103-107 (Feb.); 187-190 (March); 261-266 (April) 1950.

4. Rosenstiel, R.: Le réanimator du Docteur Rosenstiel, Presse méd. **62**:453 (March 20) 1954.

5. Mollaret, P., and Pocidalo, J. J.: Un progrés en respiration artificielle: Le respirateur portatif R. P. R. du Centre de Reanimation Respiratoire de l'Hospital Claude-Bernard, Presse méd. **65**:911-915 (May 15) 1957.

6. Huguenard, P.: Premiers essais anesthésiologiques avec le respirateur RPR, Anesth. et analg. **14**:657-678 (Aug.-Sept.-Oct.) 1957.

RESPONSIBILITIES AND METHODS IN MAINTENANCE OF HOMEOSTASIS IN UNCONSCIOUS PATIENT

Ralph Adams, M.D.
and
Aileen E. Adams, M.D., Wolfeboro, N. H.

Shock, syncope, coma, and general anesthesia are characterized by the abeyance of various reflexes, some of which are essential for survival. The inadequacy of the patient's responses to conditions that handicap respiration may be especially important. To prevent catastrophes during and after anesthesia the patient's relaxed muscles need assistance, particularly those concerned directly or indirectly with breathing; his position must be such that his airways can be kept free from blood and vomitus, and it may be necessary to remove obstructing material from pharynx or trachea by aspiration. Some patients should have periods of a few minutes at a time in prone or lateral positions lying head down for postural drainage; others who have had operations on the neck may need to be nursed sitting up. Restlessness is not always caused by pain; when it results from hypoxia, the use of narcotics is dangerous because it further depresses the protective reflexes. If prompt and effective treatment is to be available to every patient in emergency, planning is necessary. The equipment must really be at hand, for it is the seconds and not the minutes that count. The requirements include (1) an emergency endotracheal set, (2) an efficient suction apparatus, and (3) apparatus capable of administering oxygen under positive pressure.

The physician is often called in an emergency to take care of patients who have lost their normal defense mechanisms. There are various situations in which the protective reflexes are in abeyance, due to coma, injury, or a number of diseases, and the patient is in grave danger from hypoxia unless something is done to prevent it. Complex treatment is rarely called for. Application of clinical judgment and simple practical measures usually bring about a complete recovery, but lack of prompt intelligent action may mean death or survival with irreversible brain damage.

A good illustration of the type of situation that may arise is given by considering the possible postoperative complications of a routine procedure such as tonsillectomy. For purposes of description, it will be assumed that surgery and nursing care have been mismanaged and that one is called to the recovery room to find a restless young boy lying on his back with a rapid pulse rate, raised blood pressure, noisy labored respiration, and dusky lips and fingernails. On looking around quickly for the simple things needed to deal with this situation, one finds that the crank for tilting the bed is missing, the emergency equipment has been left in the operating room, and the suction apparatus is not working. As the next few minutes pass in frustrating ineffectual efforts to do something helpful, cyanosis deepens and the patients' blood pressure falls; his pulse rate becomes steadily slower and pulse volume weaker; finally, the pupils dilate, his breathing becomes feeble and eventually ceases, and the youngster has died an unnecessary death.

How could this have been prevented? Probably the sequence of events was this. As he was taken from the operating room, he developed partial airway obstruction. The loss of muscle tone from anesthesia resulted in his tongue falling back into his pharynx. The labored breathing brought about by this may have caused enough venous congestion to start some bleeding from his tonsillar fossae, adding further obstruction to his airway. Possibly he may have vomited and have retained some stomach contents in his pharynx. As his cough reflex had not returned, some of this blood and vomitus ran down into his trachea; he became dyspneic, restless, cyanotic, and died from hypoxia.

Prevention of such a catastrophe requires three simple measures. First, his relaxed muscles need assistance; his tongue should be eased forward, and the angles of his jaw pushed up to lift the base of the tongue away from the glottis. Second, his position must be such that he will not suffocate in his own blood and vomitus. Lower the head of the bed and turn him onto his side or, even better, into the semiprone position. Third, he needs aspiration of his air passages to remove the obstructing material if it is accumulating. A soft catheter should be used, with some type of side-opening at its proximal end so that suction through it can be applied

Professor of Clinical Surgery, Boston University School of Medicine, and Chief, Division of Surgery, Huggins Hospital (Dr. Ralph Adams); Staff Anesthetist, Massachusetts General Hospital, and Resident Anesthetist, Huggins Hospital (Dr. Aileen Adams). Dr. Aileen Adams is now in Sheffield, England.

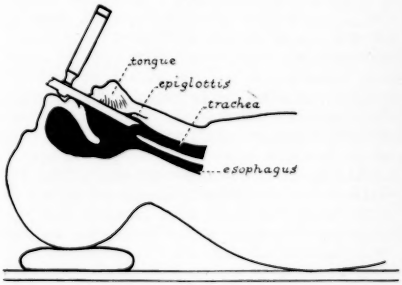
Read before the General Session of the combined meeting of the New Hampshire and Vermont Medical Societies, Dixfield Notch, N. H., Sept. 17, 1957.

intermittently and damage to the mucous membrane avoided. If he has already aspirated secretions into his lungs, he needs further postural drainage. Turn him from side to side frequently, slap his chest, and encourage him to cough. If he is sufficiently under anesthesia, the suction catheter may be passed into his trachea.

Similar situations may be met with frequently, not only postoperatively but also in the medical wards and in the emergency room. Airway obstruction may be encountered from loss of muscle tone and/or secretions of blood and vomitus occurring in induction and emergence with anesthesia; in coma from head injuries, diabetes, or barbiturate poisoning; in face or neck diseases such as goiter, jaw fractures, and laryngeal edema; in severe pulmonary disease; and in bulbar paralysis. The same principles of treatment apply to all these conditions. Patients may die not from their existing disease but from superimposed respiratory complications giving rise to airway obstruction and chronic hypoxia. Patients with fracture of the mandible, even if they are fully conscious, may become asphyxiated simply because they are unable to keep the mandible elevated and the airway patent. Laryngeal and tracheal narrowing results in typical respiratory stridor. If stridor is not relieved very promptly and conclusively by medical therapy, then immediate tracheotomy is essential. This stridor demands immediate relief. Patients of this type, as well as those who are dyspneic from pulmonary disorders, should be nursed sitting up in order to improve diaphragmatic action and lung expansion. If they have bronchial secretions, they should have periods of postural drainage in prone and lateral positions lying head down, for a few minutes at a time, and sit up in between times. Patients who have had operations on the neck should also be nursed sitting up.

Respiratory distress is often characterized by poor ventilation, either because of instability of the chest wall, as in crush injuries, or because of poor muscular action, as in paralytic disease. In other instances, inadequate oxygen transfer occurs because of pulmonary or cardiac disease. These may all be aggravated by secondary airway obstruction by secretions. Hence, the first line of treatment must include careful clearing of the air passages. This will usually give much improvement, even in the presence of diminished ventilation, as in poliomyelitis. However, if assistance to respiration is still required, a face mask and an anesthetic apparatus may be used for artificial ventilation. When many ribs are fractured, the chest wall may be stabilized by strapping with adhesive tape or by weighting with sandbags. An acute emergency sometimes follows development of tension pneumothorax, either spontaneous or traumatic. In these cases, insertion of a large-bore needle into the pleural cavity may be lifesaving.

Occasionally, these conservative measures are inadequate. Continuous bleeding, as in maxillofacial injuries; the inability to swallow secretions, as in bulbar poliomyelitis; laryngeal or tracheal edema, obstruction, or compression; and retention of bronchial secretions are urgent indications for endotracheal intubation, with either a tube with an inflatable cuff or a pharyngeal pack used to prevent contamination of the trachea. Intubation or tracheotomy is also occasionally necessary in patients with laryngeal edema, or with compression such as may be produced by retrosternal goiter. An endotracheal tube may safely be left in place for 24 hours; after that, tracheotomy is preferable. A tube in the trachea allows tracheotomy to be done without hurry and with less danger of causing hemorrhage or pneumothorax. However, if it is impossible to intubate, then emergency tracheotomy must be done. Both these procedures give good access for bronchial suction and for oxygen therapy, but it should be noted that the ability to cough effectively is lost because positive intrathoracic pressure cannot be built up.



Correct position of patient for intubation or bronchoscopy.

A practical point to be noted is that if the head is extended too far while intubation or tracheotomy is performed, a partial obstruction may be converted into a complete one. The correct position for intubation or for bronchoscopy is shown in the figure. Emergency bronchoscopy is not often indicated. If a major bronchus becomes obstructed and the patient cannot clear it by coughing and postural drainage, then bronchoscopic aspiration is advisable. When a tube or bronchoscope is passed into the trachea, vagal reflexes may result in bradycardia, hypotension, and even cardiac arrest. They should be minimized by giving atropine first, if necessary intravenously, and by using topical analgesia.

Additional Therapeutic Requirements

So far, only the establishment of a patent airway has been considered, and it is emphasized that this necessity takes precedence over all else. Once this

has been achieved, it may still be desirable to give the patient additional oxygen. A concentration of 35 to 45% oxygen in the inspired air is the optimum, and for emergency use only a nasal catheter or a face mask should be employed, since the oxygen in an oxygen tent does not reach the optimum concentration until 20 minutes after the tent has been made airtight. When using the nasal catheter, care must be taken not to insert the tip into the esophagus, or the stomach will be inflated. The flow rates required to provide the optimum oxygen concentration are 7 to 9 liters per minute with a face mask with bag, and 4 to 5 liters per minute with a nasal catheter.

If therapy is needed for more than about an hour, it is essential that the oxygen be humidified to avoid drying and crusting of bronchial secretions. A relative humidity of at least 75% must be provided, and there are several humidifiers which will do this. The steam tent may benefit patients who have difficulty in coughing up their secretions. All patients who are mouth breathers or who have tracheotomy or endotracheal intubation must have added humidity because the nasopharynx, where the normal humidification takes place, is bypassed. Positive-pressure oxygen therapy is of great value in pulmonary edema, emphysema, and in certain patients after pneumonectomy. The details of positive-pressure ventilation are important but are outside the scope of this paper. Briefly, the inspiratory pressure should not exceed 20 mm. Hg or the alveoli may be damaged. Also, the positive-pressure phase should take up not more than one-third of the respiratory cycle, and the pressure must fall to zero or below during expiration. High intrabronchial tension transmits pressure to the great veins, causing the cardiac output to fall.

The lessons to be learned from the post-tonsillectomy patient are not yet exhausted. His restlessness might have been wrongly attributed to pain, while in fact it is derived largely from hypoxia. A narcotic drug given to such a patient would be dangerous by further depressing his respiration. Extreme hypoxia will also cause circulatory depression, with rapid pulse rate and low blood pressure, which will respond to improvement in oxygenation.

However, he may have lost sufficient blood to be in genuine shock. Circulatory depression is a predominant sign in traumatic and surgical shock; burns; myocardial depression as in coronary disease, hypoxia, and overdose of drugs, including anesthesia; acute adrenal insufficiency; and acute infections such as peritonitis. It is not necessary to describe the differential diagnosis and treatment of all these conditions. Certain points warrant emphasis. First, if narcotics are to be given to patients in shock, they must be given intravenously in order to be effective, as they are not absorbed from the subcutaneous tissues because of poor circulation. Both these and anesthetic drugs must be used with caution and in small doses. Second, it is obviously better to treat shock early. Pallor, cool skin, and diminishing pulse pressure all precede a fall in blood pressure, and, if treated, hypotension can be prevented. In the anesthetized patient, tachycardia as a sign of impending shock is often absent. Third, it must be assumed that from the moment of injury all digestive and peristaltic activities cease, and patients may have a full stomach many hours after eating and may vomit during the induction of anesthesia.

In the operating room during routine surgery, a number of situations may simulate shock and cause concern until their true origin is realized. For example, the jackknife position, whether the patient is supine or lateral, may cause sudden hypotension associated with kinking and angulation of the patient. Again, the assistant may lean on the patient's neck or chest, causing respiratory difficulties, or, in intrathoracic operations, he may retract on the heart and great vessels, causing sudden disappearance of the pulse. All these are at once remedied by removing the cause. With the patient in the prone position, respiration may be embarrassed unless the abdomen is left completely free; pillows should be placed under the chest and pelvis only. Pressure on the anterior abdominal wall also causes pressure on the vena cava, resulting in engorgement of the lumbar veins, which in such operations as laminectomy makes surgery more hazardous. Air embolism must also be borne in mind as a cause for sudden change in vital signs; it occurs most frequently during intracranial operations.

Occasionally in surgery, the effects of previous drug therapy may be detrimental. If cortisone has been taken within the previous 6 to 12 months for more than a few days, then the stress of surgery may be sufficient to precipitate acute adrenal insufficiency, unless cortisone therapy is continued throughout operation. Tranquilizers such as chlorpromazine and hypotensive drugs such as reserpine and hexamethonium may have their sympathetic blocking action accentuated by anesthesia, and administration of arterenol may be necessary to maintain blood pressure.

All these considerations lead to the conclusion that, if prompt and effective treatment is to be made available to every patient in an emergency, planning is necessary to have all the equipment in readiness. Every emergency receiving room and every place where anesthesia, whether general, spinal, or local, is employed must be equipped with three things: (1) an emergency endotracheal set, (2) an efficient suction apparatus, and (3) an anesthesia or oxygen apparatus capable of administering oxygen under positive pressure. The endotracheal set should contain oral airways, suction catheters, a laryngoscope, tubes of various sizes, and a spray for topical anesthesia. Sets for tracheotomy and for treatment of cardiac arrest should be easily avail-

able. It must be emphasized that the equipment must really be at hand, because in all emergency situations it is the seconds and not the minutes that count. A few drugs should also be available on the emergency trays: atropine to dry secretions and block vagal cardiac reflexes, and some vasopressors, one with a predominately cardiac action such as ephedrine or epinephrine and one with a peripheral vasoconstrictive action such as neosynephrine. A barbiturate such as pentobarbital sodium should also be on hand to counteract the toxic effects of local analgesic agents. Should efforts at resuscitation fail and cardiac arrest result, then in these cases it is always worthwhile opening the chest and instituting cardiac massage.

Summary

Postoperative complications may arise when a patient's protective reflexes are abolished, with danger of hypoxia. It is important to maintain the airway by posture, by aspiration of secretions, and, in severe cases, by endotracheal intubation or tracheotomy. The value of being prepared in advance for all such emergencies is preeminent.

ROLE OF INTERMITTENT POSITIVE PRESSURE BREATHING POSTOPERATIVELY

Norman E. Rudy, M.D.
and
Jacques Crepeau, M.D., West Los Angeles, Calif.

958
167

With the increase in magnitude of surgical procedures and the larger number of geriatric patients coming to the surgical theater, the field of respiratory physiology assumes a role of foremost importance. Stevens states in his article on postoperative respiratory complications that the best method of management for acute respiratory problems is optimal prophylaxis. Realizing that this goal is a challenging problem, we recommend the utilization of intermittent positive pressure breathing (IPPB) both as a preventive and as a therapeutic adjuvant. The purpose of this paper is to acquaint the surgeon with the usefulness of intermittent positive pressure breathing in the prevention of postoperative complications rather than to present a statistical review of results obtained with this measure.

The frequency of pulmonary complications after surgery has been such as to indicate strongly the need of prophylactic measures, especially against postoperative atelectasis. Among etiological factors to be watched for are narcotics that suppress the cough reflex, dehydration, prolonged immobilization, and constricting dressings. These should be eliminated where possible; additional measures to be taken include chemotherapy, tracheal or bronchoscopic aspiration if necessary, and intermittent positive-pressure breathing (IPPB). For best results, IPPB should be started on the first postoperative day. Three or four treatments daily, each lasting approximately 15 minutes, are recommended. The gas recommended is 40% oxygen with either 60% helium or 60% air. It is delivered under a positive pressure of 15 to 20 cm. water in adults and 10 to 12 cm. water in children, at the rate of 8 to 10 respirations per minute. Adjuvant medication (bronchodilators, antibiotics, expectorants, detergents) can be added as aerosols to the gas. Good results in the prevention of postoperative pulmonary complications are reported in a series of 372 surgical patients, of which 144 underwent thoracic operations.

Atelectasis

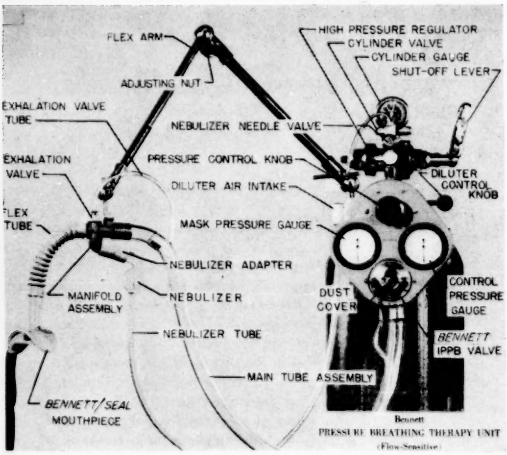
Atelectasis remains the most common of all postoperative complications.[1] Two major varieties of atelectasis exist. One is that caused by paralysis of respiratory muscles, by pleural effusion, or by other factors which decrease effective intrathoracic space. The other type is atelectasis resulting from bronchial occlusion.

Incidence and Etiology.—Various statistics have been reported regarding the frequency of postoperative atelectasis. This condition is clinically significant in 10% of cases when the operative site is the thorax or upper part of the abdomen and in 4% of the cases in which the lower part of the abdomen

is the operative site.[1] Segmental atelectasis was found in 94% of patients who developed pulmonary complications after abdominal surgery, as reported by Palmer and Sellick.[2] Swank and Smedal,[3] in a study of young soldiers, reported the incidence of atelectasis and related phenomena induced during stuporous states during deep sodium amytal narcosis. Their startling results showed the incidence of pulmonary complications to be as high as 65%.

In a series of 55 patients in whom partial gastrectomy had been performed, Stringer [4] found that 26 showed abnormal postoperative roentgenographic signs, and, of these, there were 13 with signs of lobular, partial, or massive atelectasis. Douglas [5] incriminates the following causes of atelectasis: (1) suppression of the cough reflex by anesthetic and narcotic agents, so that obstructive elements accumulate in the tracheobronchial tree; (2) dehydration and use of drying agents, so that bronchial secretions become increasingly viscid and more difficult to expectorate; (3) prolonged immobilization during and after surgery; and (4) use of constricting surgical dressings over the lower ribs for abdominal surgery and round-and-round compression dressings still used in operations on the breast.

Palmer and Sellick [6] report 31 possible etiological factors in the production of postoperative atelectasis; these fall into the following major categories: (1) reduction in bronchial caliber, (2) defective expulsion mechanism, and (3) changes in bronchial secretion.



Pressure breathing therapy unit for administration of intermittent positive pressure breathing combined with simultaneous administration of nebulizer solution of bronchodilator drug. Unit is attached to standard oxygen tank, and treatment is given with patient in sitting or prone position with use of either mouthpiece and noseclip or mask.

Diagnosis.—During the first two postoperative weeks, the triad of (1) sudden onset of fever, (2) rapid increase in pulse rate, and (3) diminished breath sounds or bronchial breathing over a lobe or segment of a lobe should alert the clinician to the probability of atelectasis. An x-ray of the chest will usually confirm the diagnosis. Some retraction of the mediastinum and diaphragmatic elevation on the involved side will be further diagnostic proof. Other signs which may prove valuable are deviation of the trachea by palpation to the affected side and limited respiratory excursion on the involved side.

Prophylactic Measures.—Methods of preventing atelectasis should be instituted in all patients who have chronic bronchopulmonary disease and/or decreased respiratory function. These methods include ample fluids, indicated chemotherapy, IPPB, and bronchoscopic aspiration when indicated. Tracheal aspiration is indicated during and immediately after the surgical procedure if secretions have been copious. During the postoperative period, the frequent turning of the patient, inducement of coughing as necessary, prevention of restriction by abdominal binders, regular deep-breathing exercises, and early ambulation is advised.

It is on the latter postoperative measures that we wish to comment in particular. Frequently, some of these are not feasible, for example, coughing by a patient who has undergone herniorrhaphy or standing by a patient with an aortic graft or adrenalectomy in the period immediately after surgery. It is in these patients and in those in whom previous bronchopulmonary disease has been present that we feel IPPB offers the most promise.

What Is Intermittent Positive Pressure Breathing?

IPPB is a technique by which the lungs are actively inflated by means of regulated positive pressure during inspiration and passively deflated to atmospheric pressure during expiration. The expiratory phase functions primarily by the elasticity of the lungs and chest wall.

The apparatus (see figure) is built around a precision flow-sensitive valve. A very low inspiratory suction opens the valve. This is immediately followed by a gradual increase of positive pressure in the mask or mouthpiece to the level set at the pressure-control gauge. At the onset of expiration, the valve closes and the pressure immediately drops to asmospheric level, thus allowing as long an expiration time as is desired without resistance.

The expired air is released through a valve at the top of the manifold, leaving a minimal dead space.

Method of Therapy.—The following plan of treatment is recommended: three to four treatments, each lasting approximately 15 minutes, should be given daily. For best results, the treatments should be instituted on the first postoperative day.

The gas used should be a mixture of helium and oxygen (60% helium and 40% oxygen) if possible. If such a mixture is not available, a mixture of 60% air and 40% oxygen should be used. Newer apparatus now in use are equipped with an air-oxygen diluter that delivers 40% or 60% oxygen mixture as well as 100% oxygen. We advocate the use of helium for the following reasons: 1. Helium is eight times lighter than oxygen and will therefore carry the bronchodilator farther down the bronchial tree, beyond obstructing secretions. 2. Most important is the fact that helium is an inert gas and only slightly diffusible through the alveolar membrane. It therefore remains in the alveoli and bronchial tree for a prolonged period, thus keeping these passages open. In atelectasis the helium passes distal to the secretions and works the occluding substance more proximally in the bronchioles, thereby enabling the patient to expectorate the material more freely. A mixture of oxygen and air is preferable to pure oxygen for the same reason: air contains nitrogen, which is less diffusible than oxygen although more diffusible than helium.

The gas is delivered under a positive pressure of 15 to 20 cm. H_2O in adults and 10 to 12 cm. H_2O in children. It is preferable to begin at a lower pressure and gradually increase to the desired level until the patient becomes accustomed to pressure breathing.

The optimal respiratory rate is 6 to 10 respirations per minute, with a long expiratory phase. The expiration should be passive and not forced, lest it cause collapse of bronchi and expiratory wheezing. Some patients may complain of slight dizziness and paresthesia, and this may be eliminated by decreasing the breathing rate.

The simultaneous administration of aerosol therapy is accomplished by means of a nebulizer attached to the apparatus. One of the following bronchodilators is used: (1) isoproterenol (Isuprel) hydrochloride, 1:20 solution; (2) cyclopentamine hydrochloride and isoproterenol (Aerolone compound solution); or (3) racemic epinephrine hydrochloride (Asthmanefrin). The cyclopentamine and isoproterenol compound is preferred in patients with coronary heart disease and hypertension because it seldom causes coronary vasoconstriction and is less likely to cause an increase in the blood pressure and pulse rate than the other two compounds. Six to eight drops of the bronchodilator is mixed with 15 to 25 drops of water, the larger amount (25 drops of water) used when helium is employed. In lieu of water a detergent, such as Tergemist (aqueous solution of the detergent, sodium 2-ethylhexyl sulfate, 0.125%, with potassium iodide, 0.1%) or Alevaire (aqueous solution of oxyethylated tertiary octylphenolformaldehyde polymer, 0.125%, with glycerin, 5%, and sodium bicarbonate, 2%), may be used in the same quantity. These agents are of particular value in patients with tenacious sputum. Antibiotics have also been given by this method, dosage and kind depending on severity and type of offending organism. Antibiotics should be given only a few days at a time. Particular caution must be exercised in those patients suspected of having allergic diathesis, and use of antibiotic aerosol solutions should probably be avoided in such instances.

Mucus and other secretions are not washed farther down the respiratory tract by the IPPB-aerosol therapy, since the peak instantaneous expiratory flow velocity is greater than the peak instantaneous inspiratory flow velocity.[7] The net result is to work the secretions outward, an expectorant-like action. The duration, frequency of use, and adjuvant medication of IPPB treatment may be adjusted to the particular needs of the patient.

At the Hospital of the Good Samaritan in Los Angeles, IPPB has been used in 372 patients after operation. Of these, 228 were general surgical and 144 thoracic surgical patients. In this series, IPPB was used only when indicated. In the entire surgical group there was a total of 18 deaths, 8 in the general surgical group and 10 in the thoracic surgical group. Four deaths in each group (1.7% and 2.7% respectively) were attributed to or associated with pulmonary complications (average of total group, 2.1%).

An extensive study recently reported by Becker and others [8] revealed that pulmonary complications were responsible for 1,263 deaths in a total of 14,010 patients operated on at the surgical clinic at the University of Giessen, Germany. This figure represents 17.2% of all deaths over a 10-year period (1945-1955) due to pulmonary complications.

Nickel and Renshaw [9] have recently reported their experience in 134 orthopedic patients requiring IPPB either preoperatively, postoperatively, or both. They reported only one case of moderately severe atelectasis, with no deaths.

Summary

The employment of intermittent positive pressure breathing (IPPB) in patients both before and after operation opens a new attack on the problems concerned with the prevention and treatment of atelectasis. Its use is particularly indicated as a prophylactic tool in those patients with chronic pulmonary

disease who are to undergo surgery and in those patients who are possible candidates for postoperative pulmonary complications.

The method of IPPB used is as follows: (1) gas mixture of 60% helium and 40% oxygen, (2) three to four treatments for 15 minutes each for five days, (3) positive pressure with 15 to 20 cm. H_2O for adults and 10 to 12 cm. H_2O for children, (4) 8-10 respirations per minute, and (5) aerosol therapy with 6 to 8 drops of a bronchodilator in 15 drops of water.

1001 Gayley Ave. (24) (Dr. Rudy).

References

1. Modersch, H. J.: Bronchoscopy in Treatment of Postoperative Atelectasis, Surg. Gynec. & Obst. **77:**435-437 (Oct.) 1943.

2. Palmer, K. N. V., and Sellick, B. A.: Prevention of Postoperative Pulmonary Atelectasis, Lancet **1:**164-168 (Jan. 24) 1953.

3. Swank, R. L., and Smedal, M. I.: Pulmonary Atelectasis in Stuporous States: Study of Its Incidence and Mechanism in Sodium Amytal Narcosis, Am. J. Med. **5:**210-229 (Aug.) 1948.

4. Stringer, P.: Atelectasis After Partial Gastrectomy, Lancet **1:** 289-291 (March 18) 1947.

5. Douglass, B. E.: Problems of Benign Bronchial Obstruction, M. Clin. North America **38:**1046-1050 (July) 1954.

6. Palmer, K. N. V., and Sellick, B. A.: Effect of Procaine Penicillin and Breathing Exercises in Postoperative Pulmonary Complications, Lancet **1:**345-346 (Feb. 16) 1952.

7. Motley, H. L., and Tomashefski, J. F.: Treatment of Chronic Pulmonary Disease with Intermittent Positive Pressure Breathing: Evaluation by Objective Physiological Measurements, A. M. A. Arch. Indust. Hyg. **5:**1-9 (Jan.) 1952.

8. Becker, W. H., and others: Fatal Postoperative Pulmonary Complications in General Surgery, Beitr. klin. Chir. **192:**203-215, 1957; abstracted, J. A. M. A. **164:**1977-1978 (Aug. 24) 1957.

9. Nickel, V. L., and Renshaw, W. L.: Experience in Reconstructive Surgery with Patients Having Respiratory Paralysis, J. Bone & Joint Surg. **39-A:**737-740 (July) 1957.

HEART SCARE, HEART SURVEYS, AND IATROGENIC HEART DISEASE

EMOTIONAL AND SYMPTOMATOLOGICAL EFFECTS OF SUGGESTING TO ONE HUNDRED SIXTY-TWO ADULTS THAT THEY MIGHT HAVE HEART DISEASE

Edwin O. Wheeler, M.D., Charles R. Williamson,† M.D.
and
Mandel E. Cohen, M.D., Boston

One hundred sixty-two individuals who, as a result of a chest x-ray examination made during the course of a tuberculosis survey, were informed that there might be something wrong with their heart were questioned to see if the suggestion that one has heart disease leads to the development of heart symptoms or symptoms of "neuroses." It is not surprising to find persons upset by this procedure, but it is of interest to find that symptoms did not develop to any extent except in persons with preexisting neurocirculatory asthenia. There was no evidence that this procedure precipitated neurocirculatory asthenia (anxiety neurosis, cardiac neurosis, neurasthenia, effort syndrome). These individuals are not necessarily a representative sample of the general population or of patients seen in doctors' offices. The relation of the findings of this study to the concept of iatrogenic heart disease is examined.

Does the suggestion that one has heart disease lead to the development of heart symptoms or symptoms of "neuroses"? Physicians have often discussed this question or reported individual patients in whom this suggestion seemed to be associated with the development or aggravation of such symptoms.[1] The widespread use of disease surveys has caused some physicians to worry about their possible role in upsetting persons and in causing heart symptoms or neuroses. These surveys, designed to detect unknown cases of disease or to determine the prevalence of disease, might conceivably make the public more aware of the symptoms of certain disorders or expose them to the suggestion that they have such disorders. The value and usefulness of such disease surveys could depend in part on their effects, either detrimental or beneficial, on the emotions and symptoms of the individuals studied.

An unusual opportunity to study the possible effects of such a disease survey arose during the Special Heart Survey of the Boston Chest X-Ray Program, in the course of which the suggestion

From the Cardiac Research Laboratory, Massachusetts General Hospital, and the Department of Medicine, Harvard Medical School.
† Dr. Williamson died Jan. 13, 1953.

was made to a large number of adults that they might have heart disease. We are reporting on the emotional and symptomological effects of this suggestion and its possible relationship to the development of heart symptoms or "neuroses." In addition certain recommendations will be made which may be of help in preventing the undesirable emotional and symptomatological effects of such surveys.

Methods and Techniques

The individuals studied were selected from persons examined in the Special Heart Survey of the Boston Chest X-Ray Program, which was a study of heart disease case finding by means of 70-mm. photofluorographic films. The details of this study have been reported elsewhere by Williamson and associates.[2]

The persons seen in the Special Heart Survey were individuals (1) who on their own volition had a chest x-ray examination made during a tuberculosis survey, (2) whose heart shadow was thought to be abnormal when the x-ray photograph was studied in the Special Heart Survey, (3) who were informed that there might be something wrong with their heart, and (4) who were requested to come to a special clinic for an examination by a cardiologist. A total of 1,154 such persons were examined in the special clinic.

The 162 subjects interviewed in this study were selected by order of registration at the individual sessions of the special clinic. They were interviewed prior to the heart examination and consecutively except when the group waiting to be interviewed became too large. When this occurred, groups of individuals were sent directly for the heart examination and thus were not included in the interview study. The interviewers did not determine the selection of subjects. No individual subject was especially included or excluded by this procedure.

In table 1 the 162 persons interviewed in this study are compared with the 1,154 persons seen in the whole of the Special Heart Survey, with regard to mean age, proportions of men and women, whites and nonwhites, and those with organic heart disease and those without organic heart disease. The 162 persons in this study did not differ significantly statistically from the whole sample of 1,154 in these regards. Seventy-one per cent of our subjects were women. Organic heart disease was diagnosed in 63% of our subjects.

The subjects were interviewed by one of the three authors (51.2% by E. O. W., 34.5% by M. E. C., and 14.3% by C. R. W.). Answers were recorded to 33 questions listed on a mimeographed form. The questions were designed to determine whether the subject (1) had in the past been told that he had heart trouble; (2) had symptoms of heart trouble; (3) had neurocirculatory asthenia (this is considered by the authors to be synonymous with anxiety neurosis, effect syndrome, cardiac neurosis, and neurasthenia); [3] (4) had new symptoms appear or the symptoms of existing disorders become worse; (5) was "upset" by the suggestion that he might have heart disease; and (6) knew what the symptoms of "heart disease" were. With regard to this sixth point, breathing troubles, chest pain, dizziness, faintness, or tiredness were considered to be symptoms of "heart disease." An individual was classed as "upset" when he answered yes to the question "were you bothered, scared, or upset," or when he appeared obviously upset to the interviewer. However, there were only three instances in which an interviewer considered a subject to be upset when the subject did not answer yes to this question. The diagnosis of neurocirculatory asthenia was based on the subject's symptoms and history.[3]

Comparison of the individuals seen by the three interviews (table 2) with regard to proportions of men and women, those over 50 years of age and those under 50 years of age, and those with organic heart disease and those without organic heart disease shows no statisically significant differences. This suggests that the three interviewers interviewed comparable groups, since these data were not dependent on the techniques of the interviewer. If in addition, the three interviewers used similar methods, one would expect that they would get similar results. This proved to be true, for, as is also seen in table 2, the examiners obtained similar results regarding the proportion of individuals who were classified as upset and who were diagnosed as having neurocirculatory asthenia.

TABLE 1.—*Patients in Study Compared with Total Patients in Special Heart Survey*

	Persons Questioned in This Study	Persons Examined in Special Heart Survey	Significance Ratio*
Total no.	162	1,154	
Age (mean)	49.0 yr.	49.1 yr.	0.06
Men, %	29.0	33.1	1.04
Women, %	71.0	66.9	1.04
	100.0	100.0	
White, %	92.6	90.0	1.03
Nonwhite, %	7.4	10.0	1.03
	100.0	100.0	
Heart disease, %	63.0	65.3	0.60
No heart disease, %	37.0	34.7	0.60
	100.0	100.0	

* Significance ratio less than 2.0 suggests that the two groups are not different from one another and that this much difference might occur within the same group by chance, i.e., odds against 20:1.

The subjects in this study were informed in the following manner that they might have heart disease. After having a chest x-ray picture made for diagnosis of tuberculosis in the Boston Chest X-Ray Program, they received a form letter stating there was need for further examination and asking them to make a telephone call to a certain number for an appointment for this examination. On calling this number, they talked with a woman who told them, "Your x-ray is clear for tuberculosis but indicates need for a heart check-up." She then asked them to come to a special clinic for a heart examination and when possible made an appointment at that time. The woman answering the telephone

tried to standardize the conversation. In most instances the verbatim details of these conversations were not recorded, but a few verbatim records were made by a third person unbeknownst to the telephoner. In a few instances, an appointment was made without mention of the heart, and occasionally more discussion took place about the heart, x-ray, or details of the heart examination, in order to persuade the subject to come to the clinic.

TABLE 2.—*Comparison of Groups Seen by Three Interviewers**

Factor	Interviewer EOW (83) %	MEC (56) %	CRW (23) %
Male	21.7	35.7	39.1
Female	78.3	64.3	60.9
	100.0	100.0	100.0
Under 50 yr.	45.8	50.0	34.8
Over 50 yr.	54.2	50.0	65.2
	100.0	100.0	100.0
Heart Disease	63.8	60.7	65.3
No heart disease	36.2	39.3	34.7
	100.0	100.0	100.0
Upset	43.9	33.9	47.8
Not upset	56.1	66.1	52.2
	100.0	100.0	100.0
Neurocirculatory asthenia	14.6	13.0	13.6
No Neurocirculatory asthenia	85.4	87.0	86.4
	100.0	100.0	100.0

* The three observers interviewed statistically similar groups as regards sex, age, and presence of heart disease and obtained statistically similar results in regard to proportion of persons classified as upset and given diagnoses of neurocirculatory asthenia. Appropriate chi-square and PQ calculations were done and in all instances indicated that the observed differences might occur by chance (odds less than 20:1) and suggested that groups and examining methods were not dissimilar.

The interval elapsing from the time he made an appointment for the examination varied from one day to three months. This interval was eight days or less for 101 of the 147 persons for whom this interval was known. The interval elapsing from the time the individual was told he might have heart trouble to the time he was examined also varied, and was eight days or less for 103 of the 127 persons for whom this interval was known.

Questionnaires were sent to each individual in this study four to six months after the special heart examination in an attempt to learn whether they received a correct impression regarding the presence or absence of heart trouble, were upset or were reassured by what they were told, were glad they came to the clinic, or had any criticism to make about the Special Heart Survey. Replies were received from 90, or 55.6%, of the 162 subjects. In some instances answers to one or more of the questions were omitted or were such as to suggest that the question was not understood. Thus complete conclusions cannot be drawn from this questionnaire information.

The data were analyzed according to standard statistical methods, using the standard error of the difference between means, the standard error of the difference between proportions, and the chi-square test with the correction of Yates for small numbers.[3] In this paper, a difference is considered to be statistically significant if the odds against its being a chance occurrence are 20:1 or greater, i. e., a significance ratio of 2.0 or greater.[3]

Results

The data from the interviews were analyzed with special attention, first, to the proportion of persons upset and the factors associated with this reaction; second, to the development of symptoms; third, to the aggravation of symptoms of preexisting disease; and, fourth, to the person's general information about the symptoms of heart disease, in addition to other factors. The information from one questionnaire was very incomplete because the subject was deaf and understood English poorly. Most of the results are based on the 161 questionnaires with adequate information. A brief summary of the answers to the follow-up questionnaire is included.

Of 161 persons, 66, or 41%, were classed as upset (table 3). The suggestion that they might have heart disease upset a larger proportion of women (51.8%) than men (14.9%), a larger proportion of the persons from 11 to 49 years of age (58.1%) than the persons of 50 years or over (26.4%) and a larger proportion of the persons who in the past had not been told they had heart trouble (46.2%) than the persons who in the past had been told they had heart trouble (29.6%). These differences in proportions are statistically significant, the significance ratio decreasing from 4.32 for sex, to 4.06 for age, to 2.02 for previous knowledge about the presence of heart disease. When all three factors were present, i. e., when the subjects were women, were young, and had not been told in the past that they had heart disease, 76.9% were upset. When all three factors were absent, i. e., when the subjects were men, were old, and had been told in the past they had heart disease, none were upset.

TABLE 3.—*Factors Related to Being Upset*

Group	No.	% Upset	Significance Ratio*
Entire sample	161	41.0	
Women	114	51.8	
Men	47	14.9	4.32
Age 11-49 yr.	74	58.1	
Age 50+ yr.	87	26.4	4.06
Not previously told had heart disease	106	46.2	
Previously told had heart disease	54	29.6	2.02
Neurocirculatory asthenia	22	68.2	
No neurocirculatory asthenia	139	36.7	2.79

* Significance ratio greater than 2.0 suggests that the observed difference is larger than might occur by chance (odds 20:1 or greater).

The subjects were divided into eight groups (table 4) on the basis of these three factors, and these eight groups were arranged in descending order of the proportion of upset persons in each group. It is seen that a greater proportion of women were upset than were men, regardless of the other

two factors; a greater proportion of young women were upset than old women, and the same of men regardless of their previous knowledge about the presence of heart disease; and, finally, a greater proportion of persons who in the past had not been told they had heart disease were upset than persons who in the past had been told they had heart disease, provided they were of the same age and sex. The number of persons in each of the eight groups is generally too few to permit useful statistical analysis. However, the fact that the data are consistent with clinical and common-sense impressions suggests that sex, age, and previous knowledge about the presence of heart disease are factors in being upset in that order of importance.

Of the 22 persons with neurocirculatory asthenia, 15 or 68.2% were upset as opposed to 36.7% of those persons without this disorder. The proportion of persons upset was at its most extreme (100%) when this fourth factor, neurocirculatory asthenia, was present in the young women without previous knowledge of heart disease. The 46 persons who delayed eight or more days before making an appointment and the 24 persons who were not examined for eight or more days after being told they might have heart trouble did not have a greater or lesser proportion of upset individuals than did those who did not experience this delay. Thirty-nine of the 66 persons who said they were upset gave the following information as evidence of this: symptoms had appeared or become worse in 13 persons, 13 had called their doctor, 10 had "trouble in sleeping," 7 had crying spells, 8 had decreased their activity, 3 had "trouble in eating," 2 had stopped smoking, and 2 had counted their pulse.

In 13 individuals (8.1%) cardiovascular symptoms appeared or the symptoms of previously existing disorders were aggravated. In 10 of these persons, 9 with neurocirculatory asthenia and 1 with angina pectoris, the symptomatology of the disorder increased. Of the remaining three individuals, two who previously had no symptoms developed awareness of heart beat, while the third, who previously had been bothered by some of the symptoms of neurocirculatory asthenia, developed more symptoms and had "probable" neurocirculatory asthenia, in our terminology,[3] at the time of the interview. Of the 22 persons with neurocirculatory asthenia, 9, or 40.9%, noted an aggravation of symptoms or the appearance of new ones in contrast to only 2.2% of those persons without neurocirculatory asthenia. Thus, while a large proportion (41%) of the individuals in the study were upset, only a few (8.1%) noted the development or aggravation of symptoms. There were no definite instances of clear-cut neurocirculatory asthenia developing in individuals who had not previously had this disorder.

Neurocirculatory asthenia antedating the present study was found in 22, or 13.7%, of 161 subjects. This is a higher prevalence than that reported for samples of the general population in the same area where it averaged 4.7%.[4] However, in another community heart survey at Framingham, Mass., Kannel, Dawber, and Cohen found the prevalence of neurocirculatory asthenia was 11.6% of 1,214 subjects. It is possible that some health surveys attract a disproportionate number of patients with neurocirculatory asthenia (anxiety neurosis). This prevalence is close to that found in this study.

Only a few of the first 69 subjects in this study mentioned any heart symptoms. Therefore it seemed of interest to ask the remainder of the subjects, 93 in number, about their knowledge of heart symptoms. This was because we wondered if the suggestion of heart disease would not lead to heart symptoms unless the subject were educated in the symptoms of "heart disease." Thirty of these persons could not name a single symptom of heart disease. The 93 persons knew a mean of only 1.03 symptoms. These people were generally not well aware of the common symptoms of heart disease.

TABLE 4.—*Relation of Sex, Age, and Having Previously Been Told or Not Told One Had Heart Disease to the Proportion of Individuals Upset*

Sex	Age (Yr.)	Previously Told About Heart Disease	Size of Group*	No. Upset	% Upset
F	11-49	No	39	30	76.9
F	11-49	Yes	14	6	42.9
F	50+	No	38	14	36.8
F	50+	Yes	22	8	36.4
M	11-49	No	13	4	30.8
M	11-49	Yes	7	2	28.6
M	50+	No	16	1	6.3
M	50+	Yes	11	0	0.0

* Two persons were omitted, one because it was not clear whether he had previously been told about heart disease, other because deafness interfered with answer.

Of the 87 persons who answered the question "What did the doctor at the Special Clinic tell you about your heart?" 75.8% had received a reasonably correct impression about the presence or absence of heart trouble, 11.5% had an incorrect impression, and 12.7% did not know. Of these 87 persons, 31.7% were not informed at the time of the clinic examination whether they had heart trouble and were left in doubt for varying periods of time until they or their physicians received a report. Five of these persons stated that they never received any information about the results of the examination. Of this group, 92.6% were glad of the opportunity to have the examination, while 7.4% made some adverse comment, generally having to do with delay in receiving information about the results of the examination, as stated before. The results of this questionnaire were not wholly conclusive.

The subjects were questioned concerning what was upsetting to them about being asked to come in for examination. They were also given an oppor-

tunity to express their fears, if any, of tuberculosis as compared with their fears, if any, of heart disease. Some of the patients' own answers throw some light on their feelings. Excerpts of verbatim statements follow.

Statements of patients who were upset: "can't have any more children if heart is bad," "couldn't sleep," "might have to quit job," "might die," "might not be able to roller skate," "thought it was tb (tuberculosis) . . . ready to go to Adirondacks . . . would have to leave college," "getting more rest since got the letter," "thought would be sent away for tb," "was scared to death for fear I had tb . . . when I found it was my heart, I danced up and down I was so happy," "thought it tb . . . couldn't have children or grandchildren to play with."

Statements of subjects who were not upset: "thought it might be due to a tight girdle," "thought it was because I wore a dress with spangles on it," "not upset . . . knew about murmur," "not upset . . . heart is a good way to go out," "it's quicker" (i. e., a cardiac death), "knew I had a murmur," "had a heavy cold when the x-ray was taken and thought something might show," "reason not frightened because I recently passed an insurance examination," "thought it was a mistake."

The initial card to the patient did not make clear whether heart disease or tuberculosis was suspected. Most patients expressed the opinion that they preferred heart disease to tuberculosis, given a hypothetical question as to preference. They felt that heart disease had good treatment these days and that tuberculosis implied being sent away, being separated from family and children. Many patients thus expressed a fear of tuberculosis because they might be sent away and separated from family and children; fear of heart disease because they believed it led to sudden death.

Comment

The individuals interviewed in this study are a good representative sample of those persons examined in the Special Heart Survey Study. They are not necessarily a representative sample of the general population or of patients seen in doctors' offices. Thus the findings in this study may not apply to other groups of people chosen in a different manner. One suspects that persons who are worried about their health and also those having symptoms would be more apt to have a chest x-ray study and agree to come in for an additional examination than would symptom-free, unworried persons. The high prevalence (13.7%) of neurocirculatory asthenia (anxiety neurosis, effort syndrome, neurasthenia, nervous exhaustion) in the group interviewed is in keeping with this belief.

Persons were classified as "upset" when they said they were upset. No attempt was made to assess the degree to which they were upset because no reliable method is known by which this may be quantitated. The suggestion, implied by the telephone call, that the individual had heart disease was obviously an upsetting one. It did not come directly from a physician but carried the weight of medical authority. How this differs in effect from a suggestion coming directly from a physician is not known.

It was not surprising to find persons upset by this procedure, but it was of interest to find that symptoms did not develop to any extent except in persons with preexisting neurocirculatory asthenia. Nor was there evidence that this procedure precipitated neurocirculatory asthenia (anxiety neurosis, cardiac neurosis, neurasthenia, effort syndrome). The internal from the time the individual was told he might have heart disease to the time of the interview was generally not many days. How soon one would expect symptoms of neurocirculatory asthenia to develop is not known. The data from the literature are not adequate to tell exactly what the incubation period is between medical words and aggravation of symptoms, but the implication seems to be that the effect is probably immediate. Being upset, however, did not seem to be related to the length of interval between stimulus, the telephone call, and our examination and interview. The follow-up questionnaires did not supply reliable information concerning the possible later development of symptoms or neurosis. Aggravation of preexisting neurocirculatory asthenia certainly occurred. This is similar to observations on the clinical course of the disorder.[4]

It was interesting to find that these persons knew little about the symptoms of heart disease. Persons who, through long periods of hospitalization or through frequent interviews with doctors, have had a chance to learn the symptoms of heart disease might respond differently than this group who had little knowledge about heart symptoms. It is possible that patients exposed to litigation, pension procedure, or unwise health propaganda might catch a few symptoms.

It is of psychological interest that more women were upset than men and that more younger persons were upset than were older persons. If one wished experimentally to upset people, then this study suggests that young women who had never been told they had heart trouble are the subjects of choice. If one wished to choose the group least likely to be upset by this suggestion, one should pick older men who have already been told they have heart trouble. This fits with a popular belief that women are more easily upset than men. The explanation of this may be actually as simple as some of the young women have stated it above, i. e., that sickness would interfere with their home life, having children, and being able to remain at home and care for them.

There are a number of reports [1] which suggest that doctors' words or advice may lead to an undefined condition called "iatrogenic heart disease." Probably this loose term usually implies that a previously well person develops a number of symptoms, which include palpitation, chest pain, dyspnea, nervousness, and faintness. There are other possibilities, however: (1) that the doctor's words have given the patient the belief that he has heart disease when he really does not, (2) that the patient's inactivity or incapacity results from the doctor's advice; or (3) that a previously existing condition such as anxiety neurosis (neurocirculatory asthenia) is made worse or the patient's incapacity from neurocirculatory asthenia is made worse by the doctor's words. Over a period of 30 years there have been published a number of papers which discuss the general subject of "iatrogenic heart disease." Fourteen of these (table 5) give some relevant data about 44 patients. In only 4 of these 44 cases is it stated that the patient had no symptoms before seeing the doctor. Thus when the literature actually gives case reports (table 5) there do not seem to be many cases in which heart symptoms or neurocirculatory asthenia are caused by doctors' words or advice in symptom-free persons. However, the clinical data from the literature suggest that preexisting symptoms or incapacities are increased. The data in the literature (table 5) are thus in close agreement with the results of our study.

TABLE 5.—*Evidence from the Medical Literature for "Iatrogenic" Heart Disease or Symptoms**

Author	Yr.	Cases, No.	Cases with Relevant Data	No Symptoms Before Seeing Doctor†	Worse After Seeing Doctor‡
Viko	1925	23	1	1	1
Kilgore	1929	1	1	1	1
Connor	1930	6	6	1	2
Ollie	1941	15	15	0	0
Wood	1941	59	1	0	1
Weiss and English	1943	3	3	0	?
Douglas-Wilson	1944	14	0	0	0
Auerback and Gliebe	1945	4	4	0	1
Drake	1948	1	1	0	0
Goldwater, Bronstein, and Kresky	1952	175	0	0	?
Weinberg	1953	1	1	0	?
Arenberg	1954	7	7	0	?
Grytting	1954	2	2	0	2
Long	1955	2	2	1§	1

* Reference 1.
† Clearly stated that patient had no symptoms before seeing doctor.
‡ Time elapsing between medical words and aggravation of symptoms was noted in three cases and was short in all three.
§ Personal communication to the authors.

There is little evidence that "iatrogenic heart disease" as usually understood (the doctor's words causing a symptom complex in previously healthy persons) actually exists. Probably the disorder described under this term is usually neurocirculatory asthenia, hysteria, or depressive disease which may have been aggravated by a doctor's words. These latter conditions are believed to be aggravated by a variety of upsetting situations [4] one of which may well be careless or thoughtless practices of a physician. The data in the literature and the results of this study support the latter idea about so-called iatrogenic heart disease, but they do not support the popular misconceptions concerning its nature, frequency, or etiology. It would be our recommendation that the term "iatrogenic heart disease" be dropped. Dropping this inaccurate term does not mean condoning careless or thoughtless words or practices of physicians or others interested in health and disease. Such practices are never acceptable and may well aggravate neurocirculatory asthenia, hysteria, or depressive disease. Hart [5] also examines critically the concept of iatrogenic heart disease and points out that patients have symptoms before seeing the physician and also that in most cases no one really knows what the physician actually told the patient.

The interviews and answers to the follow-up questionnaire suggested that the following features of the survey were special sources of worry to the subjects and certain recommendations seem indicated. 1. The original notification that the subjects received in the mail gave no indication of what was thought was wrong, and many persons assumed it was tuberculosis. A statement on the notification letter to the effect that there was no tuberculosis suggested by the chest x-ray might cause less alarm. 2. Some subjects received their notifications on Friday and had to wait until the following Monday before finding out what was suspected to be wrong in their chest x-ray, and they reported spending an anxious few days. This could be avoided by having someone answer the appointment telephone on week-ends and holidays if disturbing messages are sent out just before those times. 3. Subjects occasionally received alarming impressions from the telephone conversation. Careful instructions to the person answering the appointment telephone might avoid some of these impressions. 4. Every attempt should be made to examine the subjects as soon as possible once they are given the "heart suggestion." 5. Subjects who were not informed about the results at the end of the examination had to wait until their own physicians received a report before learning of the results, and their own physicians occasionally failed to inform the subjects. It would seem to be the responsibility of the examining physician at the special clinic to cooperate with the family physician in informing the subject about the results of the examination. If for some reason this cannot be done, the subject as well as his physician should receive a general report. Of course, unnecessary medical details should not be given to the patient.

Conclusions

From observations on 162 adults in a community survey to whom it had been inadvertently suggested that they "might have heart disease," it was con-

cluded that although such a suggestion seemed to upset and frighten almost half of the persons it did not seem to lead to symptoms of heart disease, neurocirculatory asthenia, or "neurosis" in persons previously free of such symptoms. However, a few patients with past symptoms of neurocirculatory asthenia (anxiety neurosis) or angina pectoris showed aggravation of symptoms of those conditions. It was concluded that such "suggestions" resulting in "heart scare" might aggravate the symptoms in some cases of previously existing disease.

It was of interest that the highest proportion of persons who were upset by the suggestion of heart disease were women, 51.8%; younger persons, 58.1%; and persons not previously told they had heart disease, 46.2%. The combination of persons young, female, and not "previously told" yielded the highest proportion of frightened persons, 77%. Adding neurocirculatory asthenia made this proportion even higher. It was concluded that these categories of human beings are more easily upset than others.

On the basis of patients' statements and general impressions it seems advisable, in future surveys, if only from the standpoint of courtesy and of avoiding upsetting people, to observe the following suggestions: 1. Once the question of suspected disease is brought to a patient's attention, the patient should be examined soon. Meanwhile he should have the opportunity, including weekends, to reach the office by telephone for possible explanations or reassurance. 2. Appointments or other personal information should not be sent on postal cards. 3. Reassuring statements that there is no disease or of the nature of the disease should be given as soon as possible. 4. No one giving information should be mysterious or evasive. 5. Unnecessary information about symptoms of disease should not be given to the general public.

There was no evidence, from this study, that any harm, either medical or psychiatric, follows a heart survey or that patients are dissatisfied with such studies. The data from this study support the literature on "iatrogenic heart disease," to wit, the symptoms and disability of patients with previous heart or nervous disease may become aggravated by a doctor's words, but there is little or no evidence that a doctor's words create symptoms or disease in individuals who were previously free of symptoms or disease.

This study was supported by grants from the Massachusetts Heart Association, U. S. Public Health Service, and U. S. Army Medical Department.

References

1. Viko, L. E.: Cardiac Neurosis Associated with Rheumatic Valvular Heart Disease, Am. Heart J. **1**:539-545 (June) 1926. Kilgore, E. S.: Nervous Heart, ibid. **5**:9-13 (Oct.) 1929. Connor, L. A.: Psychic Factor in Cardiac Disorders, J. A. M. A. **94**:447-452 (Feb. 15) 1930. Oille, J. A.: Cardiac Neuroses, Canad. M. A. J. **45**:1-7 (July) 1941. Wood, P.: Aetiology of Da Costa's Syndrome, Brit. M. J. **1**:845-851 (June 7) 1941. Weiss, E., and English, O. S.: Psychosomatic Medicine: Clinical Application of Psychopathology to General Medical Problems, ed. 2, Philadelphia, W. B. Saunders Co., 1949. Douglas-Wilson, I.: Somatic Manifestations of Psychoneurosis, Brit. M. J. **1**:413-415 (March 25) 1944. Auerback, A., and Gliebe, P. A.: Iatrogenic Heart Disease: Common Cardiac Neurosis, J. A. M. A. **129**:338-341 (Sept. 29) 1945. Drake, F. R.: Iatrogenic Factors in Illness, Am. J. M. Sc. **215**:103-107 (Jan.) 1948. Goldwater, L. J.; Bronstein, L. H.; and Kresky, B.: Study of 175 "Cardiacs" Without Heart Disease, J. A. M. A. **148**:89-92 (Jan. 12) 1952. Weinberg, H. B.: Iatrogenic Heart Disease, Ann. Int. Med. **38**:9-22 (Jan.) 1953. Arenberg, H.: Chest Injuries—and Iatrogenic Heart Disease, Indust. Med. & Surg. **23**:507-509 (Nov.) 1954. Grytting, G.: Iatrogene Hjertelidelser, Nord. med. **51**:99-101 (Jan. 14) 1954. Long, P. H.: Iatrogenic Aspects of Heart Disease, New York State J. Med. **55**:2637-2641 (Sept. 15) 1955.

2. Williamson, C. R.; Moore, F. E.; and Rutstein, D. D.: Heart Disease Case Finding by Means of 70 Millimeter Photofluorographic Films: Group II, Circulation **4**:652-658 (Nov.) 1951.

3. Cohen, M. E., and others: High Familial Prevalence of Neurocirculatory Asthenia (Anxiety Neurosis, Effort Syndrome), Am. J. Human Genet. **3**:126-158 (June) 1951.

4. Cohen, M. E., and White, P. D.: Life Situations, Emotions and Neurocirculatory Asthenia (Anxiety Neurosis, Neurasthenia, Effort Syndrome), A. Res. Nerv. & Ment. Dis., Proc. **29**:832-869, 1949.

5. Hart, A. D.: Iatrogenics and Cardiac Neurosis—Critque, J. A. M. A. **156**:1133-1138 (Nov. 20) 1954.

SUGGESTION ABOUT GOUT.—A study on red blood cells from galactosemic individuals revealed in a striking way that it was indeed the Gal-I-P transuridylase which was defective and that the other members of the chain were present. The same relationships were later demonstrated in liver biopsies; hence congenital galactosemia represents another example of a metabolic block. There may well be family diseases which may be more involved than a simple metabolic block. For instance, Stetten has found that patients with gout make uric acid from glycine much more readily than can be explained by the nucleotide pathway. He has therefore suggested that gout may represent a revival of the uricolytic pathway of birds. Perhaps gout is to be considered an atavism to the bird or reptile stage, an unhappy back-mutant to the "wild type" without the ability to live a wild life because the individual does not possess an avian kidney.—H. M. Kalckar, M.D., Some Considerations Regarding Biochemical Genetics in Man, *Perspectives in Biology and Medicine*, vol. 1, no. 1, 1957.

CLINICAL NOTES

MULTIPLE ANTIGEN FOR IMMUNIZATION AGAINST POLIOMYELITIS, DIPHTHERIA, PERTUSSIS, AND TETANUS

1. RESPONSE OF INFANTS AND YOUNG CHILDREN TO PRIMARY IMMUNIZATION: PRELIMINARY REPORT

Clarence D. Barrett Jr., M.D., Eugene A. Timm, Ph.D., Joseph G. Molner, M.D.
Burton I. Wilner, Ph.D., Charles P. Anderson, M.D., Harry E. Carnes, M.D.
and
I. William McLean Jr., M.D., Detroit

The use of triple antigen (diphtheria, pertussis, and tetanus combined, or DPT) in pediatric practice is well established, and its efficacy has been reviewed and discussed by Edsall [1] and Ipsen and Bowen.[2] With the accepted schedules of four-to-six-week intervals between inoculations, there has been good response to each of the three antigens in combination even when immunization is started at a very early age.[3] During 1956 the attack rates for paralytic poliomyelitis were highest in one-year-old children,[4] thereby also indicating the need for early poliomyelitis immunization. The widespread use of killed trivalent poliomyelitis vaccine in older children has been amply justified and the vaccine shown to evoke a response in infants.[5] On this basis poliomyelitis immunization of infants has been advocated [6] and the possibility of incorporation of the poliovirus antigens into DPT has aroused considerable interest. Response of infants to pertussis vaccine or DPT and poliomyelitis vaccine, physically mixed just prior to administration, or injected simultaneously into separate sites, has been reported,[7] as have laboratory studies showing animal response to mixtures.[8] However, difficulties in formulation and incompatibilities, together with the desirability of keeping the dose volume small (less than 1.5 cc.), have delayed the preparation of a desirable multiple-antigen product. As soon as these problems were resolved, the two lots of Quadrigen (combined DPT-poliomyelitis vaccine, aluminum phosphate absorbed) used in this study were prepared.

Method

The poliomyelitis vaccine components were from two lots of vaccine prepared by the formalin-ultraviolet irradiation procedure [9] and previously released for commercial distribution by the Division of Biologics Standards of the National Institutes of Health (NIH). Purified and formalin-treated diphtheria and tetanus toxoids containing purified and recrystallized benzethonium chloride (Phemerol), 1:40,000, as preservative were specially prepared. An available experimental lot of inactivated pertussis suspension prepared without preservative was employed. Concentrates of the component antigens were used so that a fully effective dose of each would be contained in the desired 0.5-cc. inoculum volume. The components were adsorbed on Holt-type aluminum phosphate adjuvant [10] so that a final concentration of 2 mg. of mineral carrier per 0.5-cc. dose would result. Thus, by use of benzethonium chloride as the preservative, concentration of the antigens, and incorporation of a mineral carrier, a potent and compatible product was achieved.

The potency of each component in the final vaccines (Quadrigen, lots B-090890 and B-090891) was determined by the standard animal test procedures prescribed by the NIH. With the exception of pertussis, each individual antigen, after combination, met or exceeded minimum requirements (see table) established for monovalent vaccines. The parent pertussis suspension, which had been stored for over one year, without preservative, had diminished in potency, and retests showed that the below-standard potency was not due to the method of preparation or the combination with the other antigens.

The subjects in which the vaccines were studied were children under current supervision in the child health clinics conducted by the Detroit Department of Health. Children, ranging in age from 2½ months to 5 years, were alternately assigned to receive one of the test vaccines; 298 contributed preinoculation blood specimens.

It was decided for this preliminary trial to follow the DPT immunization schedule in regular use by the health department to determine whether adequate response to poliomyelitis antigen could also be elicited by this customary procedure. Accordingly, all children received three monthly intramuscular 0.5-cc. inoculations of Quadrigen, and those starting the series prior to the sixth month of life were given four. Blood specimens were obtained at the time of each inoculation and one

From the City of Detroit Department of Health (Drs. Barrett, Molner, and Anderson) and Parke, Davis and Company (Drs. Timm, Wilner, Carnes, and McLean).

month after the final injection. A satisfactory series of serums for determining antibody response to the three doses was obtained from all children (224) who completed the three-dose schedule. Only 46 children of the 120 eligible for the fourth dose contributed a fifth blood specimen one month later. Special effort was made to obtain enough blood at each sampling to permit testing for poliovirus antibodies (types 1, 2, and 3), diphtheria and tetanus antitoxin, and pertussis agglutinin. When insufficient serum was obtained, priority for test was assigned in the order listed. The poliovirus neutralization antibody determinations were made in monkey kidney tissue cultures in disposable plastic panels.[11] Tests for diphtheria and tetanus antitoxin were performed according to accepted procedures,[12] and response to the pertussis antigen was determined by tests for specific agglutinin.

Animal Potency Test Results, by Standard Government Methods, with Quadrigen

Components	Quadrigen Lot B-060890	Quadrigen Lot B-060891	Minimum Requirements
Poliovirus, type* 1	1.15	0.37	0.29-0.86
2	1.39	1.48	0.25-0.75
3	0.24	0.29	0.16-0.48
Diphtheria†	3	2+	2
Tetanus‡	4(5 wk.)	3(5 wk.)	2(by 6 wk.)
Pertussis§	5.4	5.4	12(range 8-36)

* Monkey antibody response factors. Additional Standards: Poliomyelitis Vaccine, Federal Register, p. 4922, paragraph 73-100, July 3, 1956.
† Guinea pig antitoxin units per milliliter. Minimum Requirements: Diphtheria Toxoid, 4th revision, Federal Security Agency, National Institutes of Health, Bethesda, Md., March 1, 1947.
‡ Guinea pig antitoxin units per milliliter. Minimum Requirements: Tetanus Toxoid, 4th revisions, Federal Security Agency, U. S. Public Health Service, National Institutes of Health, Bethesda, Md., Dec. 15, 1952.
§ Mouse antigenic units per 1.5 ml. (Quadrigen). Mouse antigenic units per total dose (minimum requirements). Minimum Requirements: Pertussis Vaccine, 1st revision, Federal Security Agency, U. S. Public Health Service, National Institutes of Health, Bethesda, Md., Oct. 31, 1952, amendment 2.

Results and Comment

Intercurrent Illness and Reactions.—Mothers were questioned at each clinic visit and asked to report all illnesses or "reactions" by telephone. Physicians were also alerted to examine patients at each visit for evidence of local tissue response at the site of previous injections. These methods, of course, were not completely accurate in determining the frequency or intensity of reactions during the first 48 hours following the antigen injections.

During the course of the trial, in which a total of 851 inoculation exposures accumulated, there were 126 reported instances of unrelated illnesses—mostly upper respiratory infections or the common diseases of childhood—and 30 reported instances of reactions possibly due to the immunization procedure. Tenderness at the site of injection or leg soreness was reported in 16 instances; however, the femoral venipuncture procedures may have been contributory. Ten instances of fever were reported by mothers within 48 hours after an inoculation. There were four instances of reported rash: one a vesicular pruritic type observed after the third dose (a similar history was obtained after the second dose in this same child); another, an urticarial type of reaction following the second injection; two other instances were reported by mothers who gave a history of rash in their individual children.

On the decision of the clinic physician, 13 children were dropped from the study, 7 because of respiratory infections, 4 due to exposure to scarlet fever, 1 because of an urticarial reaction following injection, and 1 because of vasomotor instability following venipuncture. Another 61 were voluntarily withdrawn from the study by their parents. Over 75% of the children completed their prescribed course of primary inoculations.

Preimmunization Antibody Status.—The 298 preimmunization blood specimens were tested for diphtheria and tetanus antitoxin levels, pertussis agglutination titers, and poliomyelitis neutralizing antibodies. Of these, 52 serums showed diphtheria antitoxin levels of 0.01 units per cubic centimeter or greater, with 19 of these from children over 6 months of age. Fourteen of the 22 who had greater than 0.1 units per cubic centimeter of tetanus antitoxin were over six months of age. None of the 298 preimmunization blood specimens contained significant pertussis agglutination titers. Ninety-four of the children had triple-negative reactions for poliomyelitis; that is, they had no demonstrable antibody titers (less than 1:4) against the three types. By types, 203 were negative to type 1, 141 to type 2, and 224 to type 3. Since the half-life of

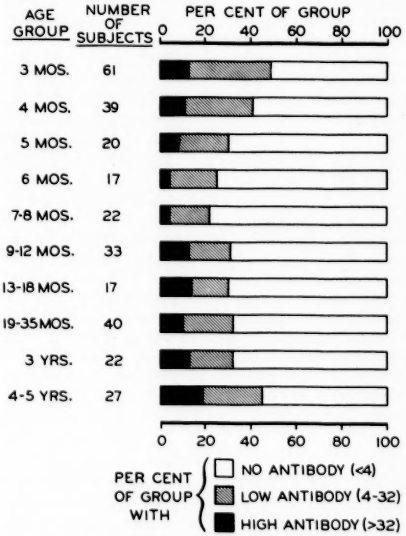


Fig. 1.—Composite preimmunization distribution of poliovirus antibody by age groups among 298 children.

poliomyelitis antibody has been reported to be one and one-half months,[13] most of the demonstrable antibody in the younger group may have been passively acquired from the mother (approximately half of the children in the study were 6 months of age or younger).

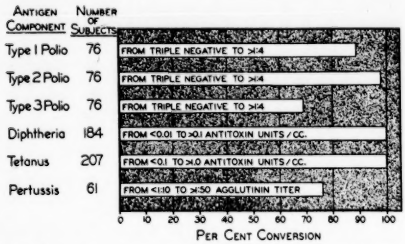

Antigen Component
Number of Subjects
Type 1 Polio 76
Type 2 Polio 76
Type 3 Polio 76
Diphtheria 184
Tetanus 207
Pertussis 61
FROM TRIPLE NEGATIVE TO ≥1:4
FROM TRIPLE NEGATIVE TO ≥1:4
FROM TRIPLE NEGATIVE TO ≥1:4
FROM <0.01 TO ≥0.1 ANTITOXIN UNITS / CC.
FROM <0.1 TO ≥1.0 ANTITOXIN UNITS / CC.
FROM <1:10 TO ≥1:50 AGGLUTININ TITER
0 10 20 30 40 50 60 70 80 90 100
Per Cent Conversion

Fig. 2.—Conversion rates for component antigens after primary immunization schedule.

When the percentages of children without antibodies for each type of poliovirus were compared on the basis of age groups, in each instance the peak level of negative reactions was found at 7 to 8 months. In general, passive antibody levels were most prevalent for type 2, and subsequent exposure seemed to occur at an earlier age, with active antibody making its appearance sooner. Exposure to type 3 was apparently not as early in this group of children, and passive antibody was also observed less frequently. At age 7-9 months 98% were without antibody to type 3. Type 1 was intermediate in passive antibody level and probable time of exposure. A composite summary of the incidence data for the three serologic types is presented in figure 1. This chart illustrates the shifting antibody pattern with age as passive maternal antibody is lost and antigenic experience through natural exposure is acquired. Up to 7 or 8 months of age the incidence of demonstrable antibody decreases progressively, while in the older children the incidence increases with age as could be expected through chance exposures to poliomyelitis antigens. It is of interest that this change in the trend of antibody pattern is correlated with the increasing independent activity of the child after 6 months of age.

Response to Primary Immunization.—No significant difference was seen in response to the two lots of Quadrigen studied, either in antibody levels or in conversion rates. Therefore, the results from the two preparations have been combined for this evaluation. Conversion rates one month after completion of the primary series of three 0.5-cc. inoculations (or four if a final blood specimen was obtained) are given in figure 2. Of the 76 subjects with triple-negative reactions for poliomyelitis completing the series, 98% showed a significant response to type 2, 89% to type 1, and 69% to type 3. Response to diphtheria and tetanus was excellent, with 100% showing protective levels of antitoxin. Only 61 postimmunization serums were available for testing for pertussis agglutinin; of these, 76% showed a titer of 1:50 or greater, a significant response considering the relatively low potency of the pertussis component. Children with preimmunization antibodies responded to the heterologous antigens in Quadrigen as well as did those without, suggesting that the "crowding-out" phenomenon [14] was not a problem in this study of combined antigens.

Since the effectiveness of the combination of diphtheria, tetanus, and pertussis is well documented in this age group, only poliomyelitis antigen response is detailed. Figure 3 illustrates that older children respond much more dramatically than do the infants. A definite response, nevertheless, is demonstrated in the 4-to-6-month group.

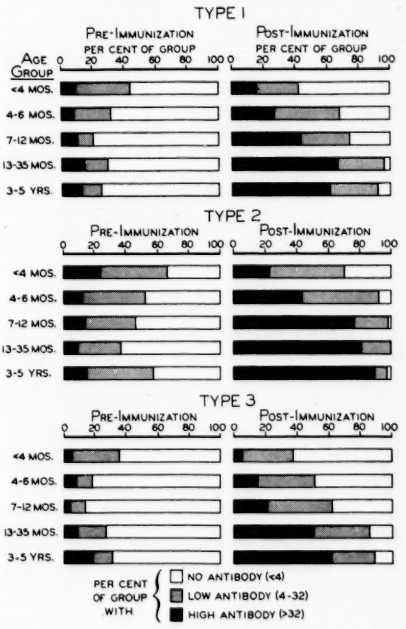


Fig. 3.—Change in poliovirus neutralizing antibody distribution in 224 children one month after three inoculations of Quadrigen given one month apart.

The low response in the 2½-month-old and 3-month-old infants is more apparent than real since there is a three-month interval between the two bleedings charted, and a marked decline in demonstrable antibody status would normally occur in this age group due to the progressive loss of material anti-

body. Therefore, the fact that antibody status is relatively unchanged is probably indicative of a vaccination response.

As has been noted, the plan of the study included a fourth inoculation for all children under 6 months of age, and the response of 46 infants one month after this fourth dose is shown in part *A* of figure 4. This final dose of antigen was quite effective, since for each serologic type approximately 80% exhibited significant levels of antibody as compared to the lower response to three doses. To show that this result was influenced by the three previous inocu-

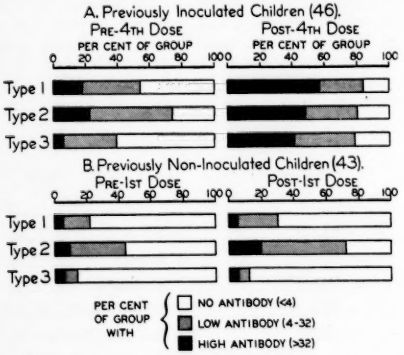


Fig. 4.—Poliovirus antibody resulting from one dose of Quadrigen in previously inoculated and noninoculated 5-month-old to 7-month-old children.

lations, the distribution of antibodies among a comparable group of 43 nonimmunized children in the same age range prior to and one month after their first inoculation has been charted in part *B* of figure 4. In this case there was no significant response to types 1 and 3 and only slight change to type 2. Not only do these data, illustrating the "priming" effect of the initial inoculations, support the above conclusion that 2-month-old and 3-month-old infants did respond, but they justify the recommendation of a fourth dose in this age group.

A significant number of the children from this study are currently receiving a stimulating dose of Quadrigen 15 to 16 months after their primary series of inoculations. Antibody evaluation studies of this booster will be part of a more complete report at a later date.

Summary

A practical multiple-antigen poliomyelitis vaccine containing diphtheria, pertussis, and tetanus antigens (Quadrigen) has been prepared, and its effects have been studied in a group of children ranging from 2½ months to 5 years of age.

Incidence of preimmunization antibodies in the studied group was lowest in the 7-to-9-month age group, indicating a need for active immunization prior to this age. Good antibody response was obtained to all antigen components of Quadrigen in children from 2½ months to 5 years of age. A fourth dose was found to be desirable for children less than 4 months of age to enhance poliovirus antibody levels.

Joseph Campau Avenue at River (32) (Dr. Carnes).

Professional assistance in obtaining blood specimens was furnished by the resident medical staff of the Children's Hospital of Michigan through Paul V. Wolley Jr., M.D., Pediatrician in Chief. Technical assistance in evaluating these serums was provided by the virus research testing group at the Parke, Davis and Company Laboratories.

References

1. Edsall, G.: Medical Progress: Active Immunization, New England J. Med. **241**:18-26 (July 7) 1949; 60-70 (July 14) 1949; 99-107 (July 21) 1949.

2. Ipsen, J., and Bowen, H. E.: Effects of Routine Immunization of Children with Triple Vaccine (Diphtheria-Tetanus-Pertussis), Am. J. Pub. Health **45**:312-318 (March) 1955.

3. Peterson, J. C., and Christie, A.: Immunization in Young Infant: Response to Combined Vaccines, Am. J. Dis. Child **81**:483-500 (April) 1951. Di Sant' Agnese, P. A.: Simultaneous Immunization of Newborn Infants Against Diphtheria, Tetanus, and Pertussis: Production of Antibodies and Duration of Antibody Levels in Eastern Metropolitan Area, Am. J. Pub. Health **40**:674-680 (June) 1950.

4. Thrupp, L. D.: Immunization of Infants with Poliomyelitis Vaccine, editorial, J. A. M. A. **166**:160-161 (Jan. 11) 1958.

5. Brown, G. C., and Smith, D. C.: Serologic Response of Infants and Preschool Children to Poliomyelitis Vaccine, J. A. M. A. **161**:399-403 (June 2) 1956.

6. Report of the Committee on the Control of Infectious Diseases, American Academy of Pediatrics, 1957. Reference 4.

7. Batson, R.: Christie, A.; Mazur, B.; and Barrick, J. H.: Response of Young Infant to Poliomyelitis Vaccine Given Separately and Combined with Other Antigens, Pediatrics **21**:1-6 (Jan.) 1958.

8. (*a*) Kendrick, P. L., and Brown, G. C.: Immune Response in Guinea Pigs and Monkeys to Individual Components of Combined Diphtheria-Pertussis-Tetanus Antigen Plus Poliomyelitis Vaccine, Am. J. Pub. Health **47**:473-483 (April, pt. 1) 1957. (*b*) Levine, L., and Wyman, L.: Factors Affecting Efficiency of Combined Prophylactics: Effect of Poliomyelitis Vaccine on Diphtheria Toxoid, J. Immunol. **79**:89-93 (Aug.) 1957. Reference 7.

9. Taylor, A. R., and others: Inactivation of Poliomyelitis Virus for Preparation of Vaccines: I. Formalin and Ultraviolet Irradiation, J. Immunol. **79**:265-275 (Oct.) 1957.

10. Holt, L. B.: Developments in Diphtheria Prophylaxis, London, William Heinemann, Ltd., 1950, p. 175.

11. Rightsel, W. A.; Schultz, P.; Muething, D.; and McLean, I. W., Jr.: Use of Vinyl Plastic Containers in Tissue Cultures for Virus Assays, J. Immunol. **76**:464-474 (June) 1956.

12. Frobisher, M.: Diphtheria Bacillus: Quantitative Determination of Antitoxin in Serum, in Diagnostic Procedures and Reagents: Technics for Laboratory Diagnosis and Control of Communicable Diseases, ed. 2, New York, American Public Health Association, 1945. Mouse Test for Titration of Pooled Guinea Pig Serum for Determination of Tetanus Antitoxin Content: Tetanus Toxin Minimum Requirements, Federal Security Agency, U. S. Public Health Service, Division of Biologics Standards, National Institutes of Health, Bethesda, Md., June 15, 1953.

13. DaSilva, M. M., and others: Transfer and Duration of Naturally Occurring and Salk Vaccine-Induced Maternal Antibodies in Newborns: Preliminary Observations on Antigenic Potency of Oral Attenuated Live-Virus Poliomyelitis Vaccine in Newborns, read before the 67th Annual Meeting of the American Pediatric Society, Carmel, Calif., June 17-19, 1957. Poliomyelitis, Research Reviews, J. A. M. A. **164**:1294-1296 (July 13) 1957.

14. Barr, M., and Llewellyn-Jones, M.: Some Factors Influencing Response of Animals to Immunization with Combined Prophylactics, Brit. J. Exper. Path. **34**:12-22 (Feb.) 1953. Chen, B. L., and others: Studies on Diphtheria-Pertussis-Tetanus Combined Immunization in Children: 1. Heterologous Interference of Pertussis Agglutinin and Tetanus Antitoxin Response by Pre-existing Latent Diphtheria Immunity, J. Immunol. **77**:144-155 (Sept.) 1956. Reference 8*b*.

NEW PLEURAL BIOPSY NEEDLE

PRELIMINARY STUDY

Constantin Cope, M.D., East Orange, N. J.

Needle biopsy of the pleura [1] was first used after it was shown by Small [2] and others [3] that open biopsy of the pleura was often a good indicator of underlying pulmonary disease. In expert hands the use of the Vim-Silverman needle has produced some very gratifying results. It has, however, two disadvantages: 1. A pleural specimen is often not obtained. 2. There is a danger of boring out a core of lung, especially when there is only a very thin cushion of pleural fluid.

In an attempt to overcome these difficulties, I have designed an instrument. Its most important unit is a curet-like needle, which has a side slot shaped as in figure 1 *C* and is set 2 to 3 mm. from the terminal blunt end; the blunt tip is closed except for a small central hole which allows, if necessary, a small needle to push out the tissue specimen. The needle stop fulfills the purpose of adjusting the size of the "bite" and of orienting the operator to the side on which the slot is located. The curet needle fits very snugly within a shorter cannula (fig. 1 *A*) which has a cutting terminal edge. The length of the slot and, hence, the bite can be varied by setting the needle stop forward for a small bite and backward for a longer cylinder of tissue. The third part of the instrument is a short beveled needle (fig. 1 *B*) which fits in the cannula (fig. 1 *A*) and is utilized to introduce the cannula to the pleural edge.

Procedure

With the patient under local anesthesia, a small nick is made in the skin with a scalpel blade (no. 11), and the cannula and needle are introduced until pleural fluid is obtained. The needle is now withdrawn slightly until gentle syringe suction does not yield any more fluid. At this point the cannula is situated just outside the pleura. The inner needle is removed, and the curet, attached to a 2-cc. syringe, is introduced to the hilt or until fluid is obtained. In order to get a good bite, the instrument is pushed laterally in the direction of the slot; this maneuver will feed pleural and subpleural tissue into the side opening. The curet is now pulled out gently until it is felt to catch the parietal pleura by its hook-like projection. At this point the cannula is advanced with the other hand with a rotating motion until it has cut a small plug of tissue (fig. 1, part 3). Now the instrument can be withdrawn with ease. The needle cuts a specimen measuring approximately 2 mm. × 3 mm. containing pleural and subpleural tissue (fig. 2).

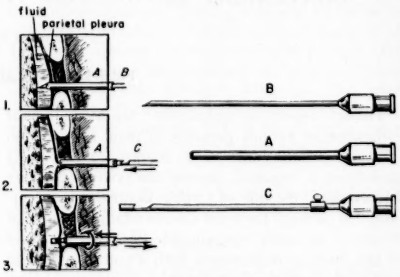


Fig. 1.—*A*, *B*, and *C*, components of biopsy needle. Parts *1*, *2*, and *3*, technique for obtaining pleural tissue.

Comment

This procedure has so far been performed on 10 patients without any morbidity. Another advantage of this instrument is that it is well adapted for use in thoracocentesis because of its blunt end. Thus, it has become my custom to tap all pleural effusions

Resident in Pulmonary Diseases, Tuberculosis Service, Veterans' Administration Hospital.

with the needle and, just before withdrawing it, to cut a small plug of tissue, thus accomplishing both duties in one operation.

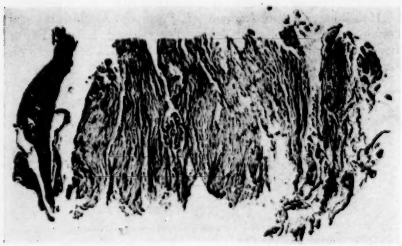


Fig. 2.—Biopsy specimen of pleural and subpleural tissue invaded by tumor cells.

Since the level of the parietal pleura is located by the hook of the curet needle, this instrument is also adapted to taking a biopsy in the absence of fluid without damage to the lung; thus tissue specimens were obtained in three patients where a pleural effusion was suspected but not confirmed on needle aspiration. It is expected that the instrument will be of equal use in peritoneal biopsy, pericardial biopsy, synovial biopsy, and the biopsy of accessible cyst-like structures.

Summary

A new type of pleural biopsy needle has been designed. In a series of 10 patients, it has been found to be safe and reliable.

References

1. De Francis, N.; Klosk, E.; and Albano, E.: Needle Biopsy of Parietal Pleura: Preliminary Report, New England J. Med. **252:**948-949 (June 2) 1955. Donohoe, R. F.; Katz, S.; and Matthews, M. J.: Aspiration Biopsy of Parietal Pleura, Am. J. Med. **22:**883-893 (June) 1957.

2. Small, M. J., and Landman, M.: Etiological Diagnosis of Pleural Effusion by Pleural Biopsy, J. A. M. A. **158:**907-912 (July 16) 1955.

3. Sutliff, W. D.; Hughes, F.; and Rice, M. L.: Pleural Biopsy, Dis. Chest. **26:**551-557 (Nov.) 1954.

CONVENIENT DEVICE FOR VENOUS PRESSURE DETERMINATION

Thomas M. Blake, M.D.
and
Patrick G. McLain, B.S., Jackson, Miss.

Though numerous techniques [1] are available for estimation of venous pressure in man, they are all either so cumbersome or so inaccurate that their usefulness is impaired. Among the systems that are widely used, the one of Lyons, Kennedy, and Burwell [1a] is perhaps the most commendable because of its use of an easily reproducible baseline: the level of the back as determined with a spirit level. The rest of their method, however, is relatively elaborate and discouraging. The simplest technique is that of Moritz and von Tabora,[1b] in which a calibrated manometer filled with saline solution is attached to a needle in an arm vein, but its lack of any clearly defined zero reference level diminishes its value considerably. To be most useful, a method for determination of venous pressure should be easy to perform and should give reproducible results with as narrow a normal range as possible. It is the purpose of this paper to describe a technique which has been devised to satisfy these criteria.

From the Department of Medicine, University of Mississippi School of Medicine.

Apparatus

The apparatus (see figure) consists basically of a rigid strip of aluminum (*A*) to which is hinged a second piece (*B*), fitted with a catch to hold it vertical. A carpenter's spirit level is attached to the first strip, and there is a centimeter scale on the upright. A sliding, hinged bar (*C*), with a stop at 90 degrees, is attached to one side of the upright and a sliding piece (*D*) with a spring clamp to the other. The whole apparatus can be folded flat when not in use and stored inconspicuously.

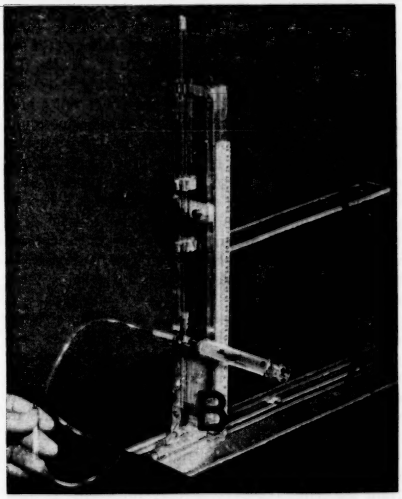
The patient lies on the bar (*A*), and the thickness of his chest at the fourth intercostal space is determined by the moving bar (*C*), which then may be folded upwards out of the way. A manometer with a three-way stopcock at its base is attached to the clamp at *D* and adjusted so that the center of the stopcock (0 on the manometer's scale) is at the desired reference level. A syringe containing isotonic sodium chloride solution (0.9 NaCl) is attached to one arm of the stopcock, and a disposable plastic connecting tube leads from the

third outlet to a needle. With the system filled with the solution and the apparatus horizontal, as determined by the spirit level, the needle is inserted into an arm vein. Venous pressure is read from the manometer after the stopcock handle has been turned to connect it with the tube leading to the vein. Repeat determinations can be done quickly by flushing and refilling the tube from the syringe reservoir and manipulating the stopcock handle.

For patients with extreme orthopnea, the whole apparatus may be set up while the head of the bed is elevated, and the patient need not be horizontal for more than the short time necessary for the fluid column in the manometer to come to rest.

Comment

The venous pressure, at least for clinical purposes, need be regarded as only a function of the right ventricular end diastolic pressure and not necessarily an absolute measure of it. For this reason, it is more important that the clinician know the range of normal values to be expected with the zero reference level he uses and that the level be clearly defined when the venous pressure is recorded than that any particular technique be insisted on. With the apparatus described here, it is equally easy to refer pressures to a zero level 10 cm. anterior to the back, as proposed by Lyons, Kennedy, and Burwell,[1a] 5 cm. dorsal to the fourth costochondral junction, as used by Friedberg,[2] or any other point of reference. If the posteroanterior diameter of the patient's chest is recorded, as well as the reference level, the value for venous pressure can be "corrected" easily for comparison with data obtained by any method.



Apparatus for determination of venous pressure.

We have chosen to use 60% of the posteroanterior diameter of the chest anterior to the back as the zero reference level. This position was suggested by work of Guyton and Greganti.[3] With allowance for varying thickness of the chest from patient to patient, it makes possible a relatively narrow range for normal values. Fifty patients without clinical evidence of cardiopulmonary disease have been studied with this technique. They were all hospitalized adults, and the posteroanterior diameter of their chests ranged from 14 to 27 cm. The mean normal venous pressure was 79.5 mm. 0.9 NaCl, with a standard deviation of 26.4 mm. and a range of 30 to 181 mm. 0.9 NaCl. Only five readings were less than 50 and three greater than 105 mm. 0.9 NaCl. In these same "normals" the hepatojugular reflux was tested by exerting firm manual pressure over the right upper quadrant of the abdomen for one minute. Response to this varied from a fall of 5 mm. 0.9 NaCl to no change. In no instance was there a rise. In five patients with no cardiopulmonary disease and in whom there was no reason to suspect that the venous pressure should change from day to day, it was found that values obtained over periods ranging up to six days did not vary more than 11 mm. 0.9 NaCl, and usually not more than 6.

Summary

A simple device for easy and accurate direct measurement of systemic venous pressure yielded the following results: Normal values in adults without cardiopulmonary disorder ranged from 30 to 181 mm. of isotonic sodium chloride solution (0.9 NaCl), with only five readings of less than 50 and three greater than 105 mm. 0.9 NaCl. The mean was 79.5 and the standard deviation 26.4. The zero reference level used was 60% of the posteroanterior diameter of the chest at the fourth intercostal space anterior to the back.

This study was supported in part by grants from the Adams County Heart Society and the Mississippi Heart Association.

References

1. (*a*) Lyons, R. H.; Kennedy, J. A.; and Burwell, C. S.: Measurement of Venous Pressure by Direct Method, Am. Heart J. **16:**675-693 (Dec.) 1938. (*b*) Moritz, F., and von Tabora, D.: Ueber eine Methode, beim Menschen den Druck in oberflächlichen Venen exakt zu bestimmen, Deutsches Arch. f. klin. Med. **98:**475-505, 1910, quoted by Lyons and others.[1a] (*c*) Burch, G. E.: Primer of Venous Pressure, Philadelphia, Lee & Febiger, 1950. (*d*) Griffith, G. C.; Chamberlain, C. T.; and Kitchell, J. R.: Simplified Apparatus for Direct Venous Pressure Determination Modified from Moritz and v. Tabora, Am. J. M. Sc. **187:**371-376 (March) 1934.

2. Friedberg, C. K.: Diseases of Heart, ed. 2, Philadelphia, W. B. Saunders Company, 1956.

3. Guyton, A. C., and Greganti, F. P.: Physiologic Reference Point for Measuring Circulatory Pressures in Dog—Particularly Venous Pressure, Am. J. Physiol. **185:**137-141 (April) 1956.

DIAGNOSTIC PROBLEMS

REMITTING OBSTRUCTIVE JAUNDICE WITH JACKSONIAN EPILEPSY

Clinical Pathologic Conference (PM 887-54), Jan. 24, 1957, from the Department of Pathology and the Hektoen Institute for Medical Research of Cook County Hospital, Chicago, presented for publication by Daniel S. Kushner, M.D., and Paul B. Szanto, M.D.

Clinical Data

A 50-year-old Negro entered Cook County Hospital "not because he felt ill but at the urging of friends." He admitted to chronic alcoholism, consuming a fifth of whiskey (757 cc.) daily. He had felt well, however, until two weeks previously when he had a chest cold, blood in his stool, anorexia, and loss of 10 lb. One week later, his sclerae turned yellow, his stools became white, and his urine brown. Since then, he had been having chills, fever, and itching of the palms and soles. He denied abdominal pain, fatty food intolerance, or recent parenteral injections.

Physical examination revealed an alert, cooperative, well-developed, and well-nourished man in no distress. His sclerae were intensely icteric. His heart was not enlarged; normal sinus rhythm was present; the aortic second sound was greater in intensity than the pulmonic second; and a soft systolic murmur was present in the mitral area. His liver extended 2 fingerbreadths below the costal margin and was tender. Rectal examination revealed a slightly enlarged prostate, external hemorrhoids, and clay-colored stool; the benzidine test was positive (1+).

Urinalysis revealed albumin 1+; a trace of sugar, bile 4+, and no urobilinogen. His hemoglobin level was 83%. His leukocyte count was 8,100 per cubic millimeter, with 74% polymorphonuclear cells, 12% lymphocytes, 7% monocytes, 5% staff cells, and 2% eosinophils. The platelet count was increased. A blood smear showed 1+ anisocytosis, polychromatophilia, targeting, evidences of toxicity, and 1 Turk cell. Roentgenograms of the chest and abdomen showed only a calcification in the aortic arch. The nonprotein nitrogen level was 27 mg. per 100 ml.

The patient was given a high-protein diet, supplemental vitamins, and 1 Gm. of chlortetracycline daily. He was discharged, condition unchanged, on the fifth hospital day. Two weeks later, he was readmitted, complaining only of generalized itching. Pertinent physical findings again consisted of intense icterus and a somewhat tender liver edge extending 2 fingerbreadths below the costal margin, without splenomegaly. Urinalysis showed a specific gravity of 1.026, albumin and sugar negative, bile 4+, urobilinogen 1+, and formed elements negative. Four subsequent specimens revealed bile (3 to 4+) and no urobilinogen. Much later in the course, bile was 2+, urobilinogen 3+. A preterminal specimen showed a trace of albumin, sugar 4+, and a trace of urobilinogen. The hemoglobin level was 59%.

The erythrocyte count was 3,640,000 per cubic millimeter. The leukocyte count was 13,350 per cubic millimeter, with 70% polymorphonuclear cells, 21% lymphocytes, 4% monocytes, 3% eosinophils, 1% basophils, and 1% staff cells. The platelet count was increased. A blood smear revealed rouleaux formation, anisocytosis 1+, polychromatophilia, targeting, and evidences of toxicity. The prothrombin time was 15 seconds (control 14 seconds). Roentgenograms of the skull revealed no evidence of trauma or sella turcica deformity; calcifications were present in the falx cerebri. Biochemical data are shown in the table. Electrocardiograms were negative.

The patient was treated with penicillin, streptomycin, and intravenous infusions. Clinically, progressive improvement was manifested by decreasing icterus and increasing appetite. A low grade fever of 99 to 100 F (37.2 to 37.8 C) persisted. The stools were brown. On the 54th hospital day, the patient suddenly developed convulsive seizures that began with paresthesias in the right arm, followed by jerking movements of the arm, spreading to the right leg. They occurred several times daily at first, lasted several minutes, and were followed by a short period of sleep. From the 59th hospital day on, the seizures occurred every five to eight minutes, lasting only a minute. Sometimes they began on the left, but more often on the right. Tonic convulsions with carpal spasm and generalized rigidity predominated, but slight clonic convulsions were also described. The patient's state of consciousness varied. At the onset of the convulsions, a neurological examination revealed no abnormalities, but as the seizures became more frequent, dilatation of the pupils and poor reaction to light were observed. The retina showed no abnormalities. The reflexes were hypoactive but bilaterally equal, and no pathological

Dr. Kushner is Associate Director of Medical Education of Cook County Hospital, and Instructor in Medicine, Northwestern University Medical School; Dr. Szanto is Director, Department of Pathology, Cook County Hospital, and Professor of Pathology, Chicago Medical School.
Dr. Steigmann is Attending Physician and Director of Therapeutics, Cook County Hospital, and Associate Professor of Medicine, University of Illinois College of Medicine.

reflexes appeared. All extremities moved with good strength. There was no nuchal rigidity. Sensation was intact.

A lumbar puncture revealed a negative Pandy's test, an initial pressure of 100 mm. H_2O, absence of spinal block, and a leukocyte count of 250 per cubic millimeter. An electroencephalogram, made during a seizure, showed spikes of seizure-discharges with stupor waves following. The discharges were generalized; there was no focal accentuation. The patient did not respond to administration of phenobarbital, diphenyhydantoin sodium, or calcium gluconate. He continued to have convulsions. Three days before he died, his temperature began to rise, reaching 106 F (41 C) on the day of his death. He died on the 63rd hospital day, about three months after the onset of his illness.

Summary of Biochemical Data

Laboratory Values	5/19	5/24	5/28	6/7	6/16	6/25	7/6	7/15	7/19	7/20
Nonprotein nitrogen, mg./100 ml.	43	40	53	...	...	...	...	...	...	74
Creatinine, mg./100 ml.	...	...	...	...	...	...	...	...	...	3.8
Fasting blood sugar, mg./100 ml.	...	...	...	...	...	...	...	...	...	910
Calcium, mg./100 ml.	...	...	...	...	...	...	...	...	11.2	11.1
Phosphorus, mg./100 ml.	...	...	...	...	...	...	...	...	5.1	...
Total protein, Gm./100 ml.	7.2	6.4	6.3	6.4	6.4	6.4	...	8.3	...	...
Cholesterol, mg./100 ml.	207	164	150	...	240	235	200	197	...	...
Cholesterol esters, %	...	22	...	...	...	...	...	...	...	...
Alkaline phosphatase, Bodansky units	9.7	8.8	9.7	12.1	16.5	17.6	33.5	19.9	...	...
Icteric index, units	221	227	199	126	131	76	49	59	...	...
Cephalin flocculation	0	...	1+	0	1+	1+	0	0	...	...
Thymol turbidity, units	5.7	...	3.5	2.8	3.4	2.6	5.7	6.0	...	...
Gamma globulin, Gm./100 ml.	1.92	...	2.02	2.16	2.65	1.89	2.16	2.24	...	...
Sodium, mEq./liter	...	...	...	...	...	...	...	...	...	145
Chloride, mEq./liter	...	...	...	...	...	...	...	...	...	102
Potassium, mEq./liter	...	...	...	...	...	...	...	...	...	5.4
Carbon dioxide combining powers, vol. %	...	...	...	...	...	...	...	...	...	22
Cerebrospinal Fluid										
Glucose, mg./100 ml.	...	...	...	...	...	...	...	...	280	...
Protein, mg./100 ml.	...	...	...	...	...	...	...	...	40	...
Chloride, mEq./liter	...	...	...	...	...	...	...	...	130	...

Clinical Discussion

Dr. Frederick C. Steigmann: With the history of alcoholism, the onset of jaundice following an upper respiratory infection, and the results of the hepatic tests, one may consider that this man had a fatty liver with jaundice due to a so-called toxic hepatitis. We frequently see alcoholics who get along well for months and even years until some external factor precipitates jaundice in a previously silent fatty liver. This may be just one more bout of alcoholic excess, an infection, a hemorrhage, or trauma. In this patient, the chest cold provided a source of infection for the precipitation of jaundice in a patient with a fatty liver. The count of 13,000 leukocytes per cubic millimeter might be used in support of the assumption of infection. The liver was enlarged and tender, as the fatty liver often is. Some such patients are even considered to have an acute abdomen. This man had pruritus, which one associates with obstructive jaundice, but cholestasis is not infrequent in a patient with a fatty liver. His initial response to tetracycline was also typical of that seen in the fatty liver syndrome. His chills and fever might have been due either to the infection that precipitated the jaundice or, more likely, to the cholangitis that so frequently accompanies biliary obstruction. The normal flocculation tests in the face of severe icterus are entirely consistent with an active fatty liver syndrome.

Despite these arguments for a fatty liver syndrome in a poorly nourished chronic alcoholic who got an infection and toxic hepatitis, we must also consider the possibility of an extrahepatic biliary obstruction. The pruritus and negative flocculations suggest an extrahepatic obstructive jaundice. Weight loss and anorexia can occur with any obstructive jaundice, but especially point toward malignancy. Chills and fever can occur with both benign and malignant common duct obstruction. The fact that the urinary urobilinogen, at first absent, later appeared intermittently suggests a fluctuating or incomplete biliary obstruction.

One of the most common causes of incomplete obstruction is cholelithiasis. Stricture is another, but there was no history of operation to suggest stricture, and cholelithiasis is extremely rare in the male Negro. Carcinoma in or near the ampulla of Vater can cause incomplete obstructive jaundice because tumors in this area are of the type that become necrotic and slough, so that intermittently bile may enter the intestinal tract; urobilinogen is formed; and there are intermittent dark and light stools with occult blood. I do not believe we can put too much importance on a 1+ benzidine test and only one stool examination, although previously the patient did note blood in the stool. We should ascertain whether the blood came from hemorrhoids or higher in the gastrointestinal tract. Blood in the stool in a jaundiced patient is often considered to result

from a hemorrhagic diathesis, but when it is associated with an incomplete biliary obstruction, it points to a carcinoma near the ampulla of Vater.

The negative flocculation tests and normal cholesterol level all fit with a diagnosis of obstructive jaundice. The low cholesterol ester determined late is indicative of liver damage, which occurs with prolonged biliary obstruction. Also any of the hepatic tests may become abnormal if biliary obstruction is associated with sepsis. In this patient, we must consider the possibility of a malignant process around the head of the pancreas and involving the ampulla which caused intermittent jaundice as a result of sloughing of the tumor, permitting blood to enter the intestinal tract. In any patient with prolonged jaundice, one must x-ray the gastrointestinal tract to exclude a gastrointestinal malignancy.

In this case, roentgenograms of the chest and abdomen were negative. The value of a search for opaque stones in KUB films of jaundiced patients is overrated. Even if one sees an opaque shadow, this is not necessarily the cause of the jaundice. The negative roentgenogram of the chest was important because if it had shown pneumonitis, we would have considered that as a possible precipitating cause of the jaundice. The next problem is that the patient appeared to improve. His icterus index was much lower at the time of his death than previously. One ordinarily assumes that this means medical jaundice, and that it is a sign of improvement. In obstructive jaundice, one sees a slow drop in the icterus index, which is usually slight and is considered to be due to a developing secondary anemia. Here the hemoglobin level fell from 83 to 59%. A fall in the icterus index from 200 to 70 cannot be due just to anemia; there must be some other explanation. In a case such as this, as the index improves one would expect the patient to improve clinically and get well, but instead, about two weeks before his death, he suddenly developed tonic and clonic convulsions which in a few days became bilateral and continued until his death, with high fever.

It is possible that the convulsions were related to hepatic coma, but in our experience generalized convulsions are rare in hepatic coma. Moreover, this patient was conscious at the onset of his seizures. Davidson [1] states he meets this combination rarely, but Adams and Foley [2] have emphasized the association. It is possible that this man had hepatic coma. Unfortunately, I cannot interpret the electroencephalographic findings. Electroencephalograms in hepatic coma (Foley) show "paroxysms of bilaterally synchronous symmetrical high voltage slow waves in the delta region." That does not fit with the description given here. The cerebrospinal fluid contained 250 cells. It is unusual to have a negative Pandy's test with so many cells present. Another possibility is that the convulsions were the result of cerebral metastases from a malignancy of the biliary tract, especially since the seizures began focally. We must also consider the possibility of a cholangiolitic hepatitis due to any one of many drugs. I have not, however, seen convulsions following this condition. These cases are usually protracted and may terminate in hepatic coma, but this patient seemed to improve before he became comatose.

Although there is no mention of abdominal pain, which he might have had with a biliary tract neoplasm, I believe that this man probably had a neoplastic lesion in the biliary tract near the ampulla of Vater, with an incomplete obstructive jaundice. This may have given him a cerebral metastasis. I would not, on the other hand, be amazed if he had a fatty liver syndrome terminating in hepatic coma.

Dr. William Meszaros: The roentgenograms were mostly negative. The skull was normal and the sella turcica not enlarged. The anteroposterior view of the skull was normal except for calcification in the falx, which is not significant. The flat plate of the abdomen showed no abnormalities. The liver and spleen shadows could not be seen. There were no calcifications in the pancreatic region. The posteroanterior view of the chest showed arteriosclerosis. The heart size was normal and the lung fields clear. All we could demonstrate radiographically was arteriosclerosis.

Dr. Paul B. Szanto: The electroencephalographic tracings showed slow waves which are supposed to be characteristic for epilepsy.

Dr. Steigmann: The electroencephalogram did not suggest hepatic coma.

Dr. S. Howard Armstrong Jr.: I would like to discuss the neurological aspect of this case. Dr. Steigmann suggested a focal cerebral lesion such as a metastasis. There were 250 unspecified leukocytes in the spinal fluid, which can occur not only with tumor or abscess but also with subdural hematoma. Although convulsions are much more common in hepatic coma, subdural hematoma is a possibility.

Dr. Steigmann: That is an excellent suggestion. Very often an alcoholic will come into the hospital with no history of injury or violence, despite the presence of bruises. This patient could have been hit or could have fallen down and sustained a subdural hematoma.

Dr. Szanto: What about the high blood sugar level before death? It went to 910 mg. per 100 ml.

Dr. Steigmann: Also, at first, he had a trace of sugar in the urine. He might have had a pancreatic lesion with a diabetic tendency. Patients with carcinoma of the body of the pancreas may have an abnormal glucose tolerance before the appearance of jaundice.

Clinical Diagnosis.—The clinical diagnosis was biliary tract neoplasm near the ampulla of Vater causing incomplete obstructive jaundice; carcinoma of pancreas with pancreatic diabetes; and focal cerebral lesion due to metastases or subdural hematoma.

Pathologist's Report

Dr. Szanto: The body was that of a well-developed, poorly nourished man with jaundiced sclerae. Both lungs together weighed 1,300 Gm. There was a marginal emphysema and the bronchi contained purulent material. Microscopically, the bronchioles contained numerous leukocytes, the picture of severe bronchitis and bronchiolitis. Horseshoe kidneys were present (350 Gm.), with a superimposed biliary nephrosis. The liver was enlarged (1,800 Gm.). The surface was smooth and the inferior margin was rounded. On section the lobular architecture was preserved and the parenchyma was green. The gallbladder was moderately distended and the cystic duct was dilated. The portal lymph nodes were enlarged and relatively firm. The hepatic and common ducts were dilated, up to 2.5 cm. in circumference. Just before its entrance into the duodenum, the common duct was compressed. The papilla of Vater was normal. The head of the pancreas was firm and nodular, and, on section, of pale gray color with loss of the normal lobular pattern. The pancreatic duct was dilated in its entire length (fig. 1), as is so typical of carcinoma of the head of the pancreas. Microscopically, the portal fields of the liver were enlarged, with evidence of portal and perilobular fibrosis. The liver cells and the liver

Fig. 1.—Extreme dilatation of pancreatic duct in its entire length.

cell plates were well preserved. Bile casts were seen in the bile capillaries and ductules, with occasional bile extravasates.

Examination of large sections taken from the head of the pancreas revealed numerous ductular structures lined by high columnar epithelium. In one area adjacent to the pancreatic duct, the pancreatic parenchyma was completely replaced by tumor tissue, consisting of pleomorphic gland-like structures. The malignant character of this tissue was also evidenced by invasion of the perineural lymphatics (fig. 2). The obstructive jaundice was

Fig. 2.—Tumor invading perineural lymphatics (hematoxylin-eosin stain, × 80).

therefore secondary to an adenocarcinoma of the head of the pancreas. How can we explain the remission of the jaundice? Such a remission may occur if the obstruction is due to a carcinoma of the papilla of Vater or of the common duct proper since, at these locations, the sloughing of the necrotic tumor tissue may alleviate the biliary obstruction. Rarely, even extensive necrosis of a carcinoma of the head of the pancreas has been associated with remission of obstructive jaundice. However, in this case, no necrosis of the tumor tissue was found.

Further study of the head of the pancreas around the tumor tissue revealed proliferating ductules with infiltration of connective tissue by inflammatory cells, merging imperceptibly with the carcinoma proper. Sections taken from the body and tail of the pancreas showed interlobular and intralobular fibrosis, lymphocytic and histiocytic infiltration (fig. 3), and marked dilatation of the ductular structures. Some of the islands of Langerhans were hyperplastic.

There is no question that the uniform cylindrical dilatation of the main pancreatic duct is characteristic of obstruction of this duct due to carcinoma originating in the head of the pancreas,[3] and, therefore, the severe pancreatic fibrosis could be explained solely on that basis. Still it seems to us that the changes in the vicinity of the carcinoma, such as fibrosis, ductular proliferation, and inflammatory

reaction, were out of proportion to the size of the carcinoma proper. While we may concede that the chronic pancreatitis directly adjacent to the carcinoma of the head of the pancreas may have resulted from the tumor, it is also possible that in this case the carcinoma developed in a preexisting chronic relapsing pancreatitis. The subsidence of a recent exacerbation of the chronic pancreatitis in the head of the pancreas may explain the remission of the jaundice. Ductular proliferation, which occurs in chronic pancreatitis and in diabetes, has been considered by some as a precancerous lesion. This may explain the frequency of carcinoma of the pancreas in diabetic patients.[4]

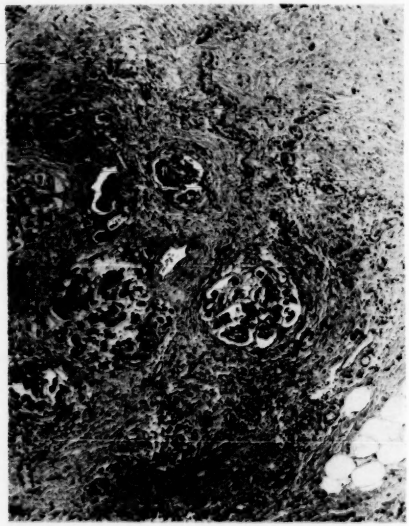


Fig. 3.—Extensive pancreatic fibrosis, with inflammatory reaction and remnants of pancreatic acini.

The brain (1,300 Gm.) showed thickened meninges, cortical atrophy, and dilatation of the lateral ventricles. This appearance of the brain is that which is frequently seen in chronic alcoholics. Microscopically, small focal perivascular hemorrhages were seen in the fibrotic meninges and atrophic cortex. Sections taken from the hypothalamus, mesencephalon, pons, and medulla oblongata revealed old and recent lesions. The older changes were characterized by fibrotic thickening of the small vessels, gliosis, and decrease in number of the nerve cells in the mamillary bodies. The superimposed recent changes were perivascular hemorrhages and varicose dilatation of the capillaries and other small vessels. This recent picture resembled that in Wernicke's hemorrhagic polioencephalopathy which has been superimposed upon a previous insult of the same type.[5] The cerebellum showed degenerative changes in the granular cell layer; very recently it has been pointed out that this is a characteristic lesion occurring in alcoholic polioencephalopathy, as an end-product of previous episodes of superior hemorrhagic polioencephalopathy.

Pathological Diagnosis.—The pathological diagnosis was adenocarcinoma of the head of pancreas; chronic pancreatitis; obstructive jaundice secondary to adenocarcinoma of the head of pancreas and chronic pancreatitis; and superior hemorrhagic polioencephalopathy (chronic and acute).

Comment

Dr. Szanto: There are three target organs of malnutrition in chronic alcoholism: liver, pancreas, brain. In this instance, the liver showed only changes secondary to biliary obstruction, and no cirrhosis. The possibility has been considered that the carcinoma of the pancreas developed superimposed on a chronic pancreatitis. Chronic relapsing pancreatitis occurs frequently in chronic alcoholics.[6] The third target organ of alcoholic malnutrition is the brain. Atrophy of the cortex, thickening of the meninges, old and recent vascular changes in the brain stem occur in chronic alcoholics. The migratory type of Jacksonian epileptic-like seizures can be explained by the diffuse morphologic involvement of the brain. Some of these changes may be the direct result of alcohol, others (especially the changes in the brain stem known as superior hemorrhagic polioencephalopathy of Wernicke) are due to malnutrition, especially deficiency of the vitamin B complex.[7] Experimentally, similar lesions have been produced by thiamine deficiency.

References

1. Davidson, C. S.: Hepatic Coma, in Advances in Internal Medicine, vol. 7, edited by W. Dock and I. Snapper, Chicago, Year Book Publishers, Inc., 1955, pp. 33-63.

2. Adams, R. D., and Foley, J. M.: Neurological Disorder Associated with Liver Disease, A. Res. Nerv. & Ment. Dis., Proc. (1952) **32**:198-237, 1953.

3. Bell, E. T.: Carcinoma of Pancreas: I. Clinical and Pathologic Study of 609 Necropsied Cases: II. Relation of Carcinoma of Pancreas to Diabetes Mellitus, Am. J. Path. **33**:499-523 (May-June) 1957.

4. McKittrick, L. S., and Root, H. F.: Diabetic Surgery, Philadelphia, Lea & Febiger, 1928, p. 250.

5. Victor, M., and Adams, R. D.: Effect of Alcohol on Nervous System, A. Res. Nerv. & Ment. Dis., Proc. (1952) **32**:526, 1953.

6. Comfort, M. W.; Gambill, E. E.; and Baggenstoss, A. H.: Chronic Relapsing Pancreatitis: Study of 29 Cases Without Associated Disease of Biliary or Gastrointestinal Tract, Gastroenterology **6**:376-408 (May) 1946.

7. Alexander, L.: Wernicke's Disease: Identity of Lesions Produced Experimentally by B_1 Avitaminosis in Pigeons with Hemorrhagic Polioencephalitis Occurring in Chronic Alcoholism in Man, Am. J. Path. **16**:61-70 (Jan.) 1940.

COMMITTEE ON COSMETICS

Report to the Committee

The following paper was presented at the Symposium on Cosmetics, in New York City, Dec. 27, 1956. This second symposium was sponsored by the Committee on Cosmetics in cooperation with the Section on Pharmacy at the 123rd annual meeting of the American Association for the Advancement of Science. This is the final in a series of papers, the first of which appeared in THE JOURNAL *for Feb. 8, page 638, and the second of which appeared in* THE JOURNAL *for Feb. 15, page 771.*

VERONICA LUCEY CONLEY, *Secretary.*

CONTROL OF AXILLARY SWEATING AND OF BODY ODOR

Franz Herrmann, M.D.
and
Marion B. Sulzberger, M.D., New York

958
167

Apocrine and Eccrine Sweat

Axillary sweat is composed of two principal constituents: (1) the more free-flowing sweat produced by the eccrine glands and at times perhaps also by the apocrine glands, and (2) the more viscous product of the apocrine glands, which largely resemble the milk glands. Like Rothman,[1] we have expressed the opinion that the apocrine glands may produce two different types of sweat, one more viscous, the other less viscous and thus more like the product of the eccrine glands.[2] In any case, the major portion of excessive sweating from the axillas is made up of the eccrine type of sweat, whereas only a minor portion is of the milky apocrine type.[2a, b] Although it is still controversial whether the quantity of apocrine sweat itself may not play a greater role than has been suggested, for all practical purposes it is mainly the eccrine sweat that must be controlled in combating excessive sweating in the armpits. Since this control is effected almost exclusively by external means, we shall confine ourselves to the discussion of external measures for the reduction of eccrine sweat in the axillas.

External Measures for Reduction of Sweat in Axillas

The common experience of tens of millions of consumers, as well as a great deal of experimental work, prove that aluminum salts are able to diminish axillary sweating with considerable regularity and consistency. Nevertheless, in extreme degrees of axillary hyperhidrosis, these salts may be washed off and thus be less effective.

On the other hand, Shelley's[3] experimental result indicating that aluminum chloride is ineffective in strong axillary hyperhidrosis might, to some degree, be based upon the fact that the test indicator which was used, namely, starch-iodine, becomes less sensitive at higher ranges in pH. It may, therefore, indicate less fluid than is actually present in the untreated control axilla with a pH sometimes considerably above 7. However, in the axilla treated with an aluminum salt as acid as aluminum chloride, in which the pH may range well below 4, the sensitivity of the indicator is not diminished, and all the sweat present will be recorded.

A number of investigators, including Richardson and Meigs,[4] Fredell,[5] Hopf,[6] and Helton, Daley, and Erwin,[7] as well as our own group, observed distinct inhibition of axillary sweating in the majority of the test subjects after various aluminum salts had been used. In these investigations we took sweat-prints on filter-paper squares impregnated with a powder mixture containing bromphenol blue.[8] One of the advantages of this method is the fact that the readings are less liable to errors by shifts in pH than those obtained with starch-iodine and several other indicators. The antihidrotic effect of aluminum salts was more pronounced in subjects with moderate sweating than in those with strong axillary hyperhidrosis; however, even in the latter some effect was usually noticeable. Practically, the question simply boils down to "a matter of degree," as pointed out by another investigator.[9]

Like other groups,[10] we obtained a significantly stronger antiperspirant effect with a watery solution of aluminum chloride in combination with a wetting agent than with aluminum chloride alone. This difference was apparent in the axillas, as well as on the palms and soles, but less distinct on the trunk. These findings suggest that the addition of suitable wetting agents increases the contact of aluminum salts with the stratum corneum, especially at and about the sweat pores, in the areas where the salts otherwise tend to be washed off by the

From the Department of Dermatology and Syphilology of the New York University Post-Graduate Medical School and the Skin and Cancer Unit of the University Hospital.

sweat. Many, if not all, of the purchasable antiperspirant aluminum salt preparations today contain a wetting agent.

Considering the tremendous number of daily applications of aluminum salt antiperspirants to the axillas, the incidence of untoward side-effects is relatively rare. In addition to occasional micropapular dermatoses (similar to prickly heat) and the more deep-seated folliculopapular skin eruptions, there are occasional direct irritant effects and the very rare cases of allergic eczematous contact dermatitis. The tendency to develop folliculopapular eruptions is an individual matter.[11] The individual predisposition, however, seems to occur not only as a sporadic incident but also as a familial trait, for of a total of about a dozen subjects in whom we observed folliculopapular eruptions from antiperspirants, three were siblings of one family, two of another, and two of a third family.

The mechanism of action underlying the reduction of eccrine sweat delivery by aluminum salts is not yet entirely clear. It appears to result from a combination of factors, important among which are a mild inflammatory reaction with edema, expansion of the horny layer at the ductal orifices, and consequent narrowing of the pores.

Among a few less effective agents studied, a simple powder mixture of 3% salicylic acid and 97% talcum produced some reduction of axillary sweating.[2c] Exchange resins also showed a mild antiperspirant effect.[12] This effect was distinctly weaker with anion exchange resins than with cation exchange resins.

More recently, zirconium salts have been incorporated in several antiperspirant preparations. Certain, not altogether rare, papular axillary eruptions of a new type, microscopically resembling tuberculoid granulomas, beryllium granulomas, or silicon granulomas, were attributed to the sodium zirconium lactate which was present in some of the newer stick preparations.[13] Saunders suggests that these granulomas are caused by apocrine duct rupture.[14] Shelley and Hurley, however, recently demonstrated the formation of epithelioid cell granuloma as a result of specific allergic sensitization to zirconium salts.[15]

Causes of Osmidrosis

It is difficult to characterize a body odor as agreeable or disagreeable, since in the domain of olfactory impressions one man's meat is certainly another man's poison—what is attractive or indifferent to one nose is disgusting to another, what is perceptible to one sniffer cannot be detected by another. Nevertheless, certain odors are almost unexceptionally disagreeable to the human olfactory sense. Unpleasant body odors, as a rule, are due to a combination of factors, including changes in the composition of sebum, of keratin, and of the sweat. Microbial activity may well be the major factor responsible for widespread decomposition of each of these three substrates. Malodorous sweating is termed bromhidrosis or osmidrosis.

Generalized bromhidrosis may occur in certain metabolic or infectious diseases.[16] Moreover, certain drugs and even foods may render the sweat odorous, notably valerian, asafetida, garlic, and onions.[16] In a limited number of tests, we have not been able to show that such odors are significantly reduced by the intake of chlorophyllin.

As shown by Shelley and others,[3] apocrine sweat decomposed by microbial activity is the main offender in localized bromhidrosis of the axillary areas. The same investigators emphasized the absence of odor in native apocrine sweat, since they did not detect any odor in freshly produced apocrine sweat in the disinfected axillas of their subjects.[3] Although these observations, by and large, agree with those of Killian and Panzarella,[17] the question of the natural occurrence of odorous substances in "sterile" apocrine sweat appears to require further exploration.

By means of paper chromatography Nitta and Ikai[18] demonstrated that, of the lower unsaturated fatty acids, those with four or more carbons were present in greater quantity in persons with axillary osmidrosis than in persons without osmidrosis. These observers attribute axillary osmidrosis to the combined function of a relatively large amount of apocrine sweat plus its original composition and the action of enzymes, which emanate from microorganisms and alter the composition of the sweat toward formation of the unsaturated fatty acids with four or more carbons.

Whatever may be one's stand on the absolute lack of odor of native apocrine sweat, it is certain that effective deodorants include those which interfere with the growth of bacteria on the skin and in the hair follicles. The aluminum salts show antibacterial activity,[19] and even shaving considerably reduces the axillary odor,[3] presumably because the hairs favor the settlement of bacteria. In addition, the hairs are sites of adherence of odor-producing material. Externally applied antibiotics have proved distinctly effective in controlling axillary odor.[20] Moreover, soaps containing hexachlorophene, which is known to every layman today, or soaps containing tetramethylthiuram disulfide (TMTD) produce a deodorant effect in the axillas for many hours in most persons.[21]

Another category of agents of some promise is that of the exchange resins, as reported by Thurmon and Ottenstein[22] and by Ikai.[23] In agreement with Ottenstein's results in vitro, we obtained a distinct decrease in the pH of the axillary skin by means of cation exchange resins.

Conclusions

In conclusion, it may be stated that the problem of how aluminum salts reduce axillary odor still merits further experimentation; it is possible that these salts may diminish also the outpouring of apocrine sweat. Our microscopic findings [11] indicate that single applications of aluminum salt preparations to the axillas produce changes which have much in common with the features of apocrine sweat retention obtained subsequently by Hurley and Shelley upon massive experimental obstruction of the apocrine ductal orifices with concentrated nitric acid or by electrodesiccation.[24] The common features include dilatation of the apocrine tubules, compression atrophy of the epithelium, and cellular casts in the tubular lumens. In their aggregate, the findings suggest that the mechanisms by which the aluminum salts (and perhaps also certain other deodorant preparations) act in the control of axillary odor may, in addition to the reduction of microbial activity, include a reduction in the actual amount of apocrine discharge to the skin surface.

References

1. Rothman, S.: Physiology and Biochemistry of the Skin, Chicago, University of Chicago Press, 1954.

2. (*a*) Shelley, W. B., and Hurley, H. J., Jr.: Symposium on Sweat Apparatus: Methods of Exploring Human Apocrine Sweat Gland Physiology, A. M. A. Arch. Dermat. & Syph. **66:**156 (Aug.) 1952. (*b*) Shelley, W. B., and Hurley, H. J., Jr.: Physiology of Human Axillary Apocrine Sweat Gland, J. Invest. Dermat. **20:**285 (April) 1953. (*c*) Sulzberger, M. B., and Herrmann, F.: Clinical Significance of Disturbances in Delivery of Sweat, Publication 178, American Lecture Series, monograph in Bannerstone division of American Lectures in Dermatology, edited by A. C. Curtis, Springfield, Ill., Charles C Thomas, Publisher, 1954. (*d*) Herrmann, F., and Kanof, N. B.: Physiologic and Pharmacologic Aspects of Sweating, in Cosmetics: Science and Technology, edited by E. Sagarin, New York, Interscience Publishers, Inc., 1957, chap. 46, p. 1176.

3. Shelley, W. B.; Hurley, H. J., Jr.; and Nichols, A. C.: Axillary Odor: Experimental Study of Role of Bacteria, Apocrine Sweat, and Deodorants, A. M. A. Arch. Dermat. & Syph. **68:**430 (Oct.) 1953.

4. Richardson, E. L., and Meigs, B. V.: Method for Comparative Evaluation of Antiperspirants, J. Soc. Cosmet. Chem. **2:**308 (Dec.) 1951.

5. Fredell, W. G.: Summary of Discussions on Mechanism of Antiperspirant and Deodorant Activity, J. Soc. Cosmet. Chem. **7:**273 (May) 1956.

6. Hopf, G.: Desodorisierende Massnahmen in der Korperpflege, J. Med. Kosmet. **1:**6, 1955.

7. Helton, E. G.; Daley, E. W.; and Erwin, J. C.: Zirconium Oxychloride, New Ingredient for Antiperspirants, Proc. Scient. Sec. Toilet Goods A., no. 26, p. 27, Dec., 1956.

8. Herrmann, F.; Prose, P. H.; and Sulzberger, M. B.: Studies on Sweating: IV. New Quantitative Method of Assaying Sweat-Delivery to Circumscribed Areas of Skin Surface, J. Invest. Dermat. **17:**241 (Oct.) 1951. V. Studies of Quantity and Distribution of Thermogenic Sweat Delivery to Skin, ibid. **18:**71 (Jan.) 1952. Reference 2*c*.

9. Klarmann, E. G.: Chemical and Bacteriological Aspects of Antiperspirants and Deodorants, J. Soc. Cosmet. Chem. **7:**85 (March) 1956.

10. Manuila, L.: Traitement medicamenteaux local de la transpiration axillaire, Dermatologica **100:**304, 1950. Brun, R.: Experiences sur la transpiration: A propos du traitement de l'hyperhidrose plantaire, ibid. **111:**316 (Nov.) 1955.

11. Sulzberger, M. B.; Zak, F. G.; and Herrmann, F.: Studies of Sweating: II. On Mechanism of Action of Local Antiperspirants, Arch. Dermat. & Syph. **60:**404 (Sept.) 1949. Reference 2*c*.

12. Herrmann, F., in discussion on Fredell.[5]

13. Weber, L. F., and others: Granuloma of Axillas, Correspondence, J. A. M. A. **162:**65 (Sept. 1) 1956. Rubin, L.; Slepyan, A. H.; Weber, L. F.; and Neuhauser, I.: Granulomas of Axillas Caused by Deodorants, ibid. **162:**953 (Nov. 3) 1956.

14. Saunders, T. S.: Granulomas of Axillas Caused by Deodorants, A. M. A. Arch. Dermat. **76:**619 (Nov.) 1957.

15. Shelley, W. B., and Hurley, H. J.: Experimental Evidence for an Allergic Basis for Granuloma Formation in Man, Nature **180:**1060 (Nov. 16) 1957.

16. Ormsby, O. S., and Montgomery, H.: Diseases of the Skin, ed. 8, Philadelphia, Lea & Febiger, 1951.

17. Killian, J. A., and Panzarella, F. P.: Comparative Studies of Samples of Perspiration Collected from Clean and Unclean Skins of Human Subjects, Proc. Scient. Sec. Toilet Goods A., no. 7, p. 3, May, 1947.

18. Nitta, H., and Ikai, K.: Studies on Body Odor: I. Separation of Lower Fatty Acids of Cutaneous Excretion by Paperchromatography, Nagoya M. J. **1:**217 (Oct.) 1953.

19. Hocs, S.: Oligodynamics of Metallic Salt Solutions, Helvet. chir. acta **13:**153, 1930. Meyer, E., and Vicher, E. E.: Germicidal Activity of Alcohol, Hydrochloric Acid and Aluminum Potassium Sulfate: Their Effect on Cutaneous Flora, Arch. Surg. **47:**468 (Nov.) 1943. Killian, J. A.: Evaluation of In-Vitro and In-Vivo Methods of Testing Deodorants with Particular Reference to Chlorophyll and Its Derivatives, J. Soc. Cosmet. Chem. **3:**30 (March) 1952. Strauss, J. S., and Kligman, A. M.: Bacteria Responsible for Apocrine Odor, J. Invest. Dermat. **27:**67 (Aug.) 1956. Blank, I. H.; Moreland, M.; and Dawes, R. K.: Antibacterial Activity of Aluminum Salts, Proc. Scient. Sec. Toilet Goods A., no. 27, pp. 24-28, May, 1955. References 3 and 9.

20. Shelley, W. B., and Cahn, M. M.: Effect of Topically Applied Antibiotic Agents on Axillary Odor, J. A. M. A. **159:**1736 (Dec. 31) 1955.

21. Baer, R. L., and Rosenthal, S. A.: Germicidal Action on Human Skin of Soap Containing Tetramethylthiuram Disulfide, J. Invest. Dermat. **23:**193 (Sept.) 1954.

22. Thurmon, F. M., and Ottenstein, B.: Studies on Chemistry of Human Perspiration with Especial Reference to Its Lactic Acid Content, J. Invest. Dermat. **18:**333 (April) 1952.

23. Ikai, K.: Deodorizing Experiments with Ion Exchange Resins, J. Invest. Dermat. **23:**411 (Dec.) 1954.

24. Hurley, H. J., Jr., and Shelley, W. B.: Apocrine Sweat Retention in Man: I. Experimental Production of Asymptomatic Form, J. Invest. Dermat. **22:**397 (May) 1954. Shelley, W. B., and Levy, E. J.: Histologic Observations on Human Apocrine Sweat Gland in Health and Disease, ibid. **25:**249 (Oct.) 1955.

COMMITTEE ON MEDICOLEGAL PROBLEMS

FOLLOW-UP STUDY OF FATAL PENICILLIN REACTIONS

SPECIAL REPORT

Abraham Rosenthal, M.D., New York

During the years 1952 and 1953, the Office of Chief Medical Examiner of the City of New York investigated eight fatal reactions after penicillin injection, and I published a report in the *New York State Journal of Medicine* of May 15, 1954, entitled "Eight Fatal Anaphylactic Reactions to Penicillin."[1] This article was immediately widely reported in the lay press in many lands and languages. In the Sept. 4, 1954, issue of THE JOURNAL there appeared a full abstract of the article. In the November, 1954, issue of *Coronet* magazine, a lay science writer abstracted the original article without our knowledge and called it "Penicillin Turns Killer."

From the time of the publication of the original article, a large amount of mail was received both from the medical profession and from the allied professions and laity. All the above is mentioned because by the time the stir this article created wore off, it was hoped that we would have less occasion to encounter fatal penicillin reactions.[2] However, the reason for this report is that, although for a while it seemed that the desired effect of the 1954 publication was being achieved, it has turned out that instances of fatal reactions to penicillin are still occurring.[3] We have in the Office of Chief Medical Examiner of the City of New York for the years 1954, 1955, and 1956 accumulated 18 more deaths. The figures for 1957 are not complete, but we know of at least 4 more, thus making a total of 22 since our last report and, with those published, a total of 30 fatal reactions from penicillin in less than five years.

One readily concedes that in a city like New York, with a population of over 8 million people, there must be countless doses of penicillin administered and that these deaths comprise an infinitesimal figure in the over-all use and unquestioned usefulness of this drug.[4] However, without denying the fact that our population would be far smaller were it not for the almost miraculous good wrought by penicillin, it cannot be overlooked that in many instances an overwhelming reaction to penicillin is preventable.

Since this report is in the nature of a follow-up to the previous publication, it might be of interest to comment on some changes in our thinking since then. It was stated, in 1954, that "no parenteral use of penicillin should be undertaken without first having ascertained the history of previous sensitivity," or that of any type of allergy. At that time it was considered safe to offer the drug by mouth when there was doubt about the possibility of a reaction by its parenteral use. This idea must be changed because now there are reports of fatal and near-fatal reactions not only from orally administered penicillin but even from sucking on a lozenge containing only 20,000 units.[5] Recently there appeared a report from an Army medical installation in Occupied West Germany[6] on the use of a 15-minute intradermal and/or conjunctival aqueous penicillin test, with use of the solution to be given to the patient in the absence of any reaction. There were no fatal reactions. This technique is practical under conditions comparable to an Army hospital, but it is hard to picture the busy general practitioner on his rounds of house calls skin-testing every squirming youngster when in doubt. That it can be done there is no question, but one must be practical. In a busy office, however, it would seem simple enough to make up a fresh vial of 300,000 units of aqueous penicillin daily and to use it for intradermal or conjunctival testing, with a control skin test with the diluent.

But even this method has its pitfalls, for two months after the publication of the article, there appeared a report in the form of a letter to the editor of the *New England Journal of Medicine* from a physician who, in using the conjunctival test, as described in the Army report, had a near-fatal reaction in his office.[7]

Since 1954 the literature has become filled with reports of the discovery and clinical use of numerous new antibiotics, some of which have an unusually wide spectrum of applicability. Although penicillin is the least toxic, is bactericidal, and is about the least expensive of all antibiotics, we nevertheless have a choice of any one of many, such as erythromycin; carbomycin; novobiocin; streptomycin and dihydrostreptomycin; the tetracyclines, that is, tetracycline, chlortetracycline, oxytetracycline; chloramphenicol; bacitracin; neomycin; polymyxin B; viomycin; cycloserine; tyrothricin (for local use); and ristocetin (specifically against staphylococcic infection, this organism being the plague of our modern antibioticized exist-

Assistant Medical Examiner, City of New York.

ence, especially in hospitals). It should be kept in mind, however, that, of the reactions caused by 809 preparations reported in December, 1957, by the Food and Drug Administration, 793 were caused by penicillin, with 72 deaths, and 16 reactions were caused by streptomycin, dihydrostreptomycin, chloramphenicol, and tetracycline, with 2 deaths.[4]

It is not the province or purpose of this presentation to discuss advances in treatment with antibiotics. One should not under any circumstances abandon the use of penicillin, a drug to which countless numbers owe their lives despite a few tragic mishaps, but greater care must be exercised in its use so that its lifesaving work may go on unimpeded. When there is any question about whether a patient is sensitive to the drug or where there is a history of allergy, as there may well be in one out of seven people,[8] one might consider using another antibiotic in its place unless bacteriological studies and in vitro sensitivity tests indicate penicillin to be the only drug capable of affecting a given organism. In such an instance, there have been developed techniques of desensitization which, although time-consuming and meticulous, have applicability.[9] The patient has to shoulder some of the responsibility for these mishaps. How often does he say to the physician, "Just give me a shot of penicillin and I'll be OK"? However, the physician must be the sole and final judge as to what medication is needed.

958
167

Statistical Survey

For statistical purposes, we have included in our present study the 8 cases originally published, thus making the total number of cases 30. In a general way, the following facts may be gleaned as to age, sex, and race. The youngest was one month old, the oldest 66 years old, and the average age 33.8 years. There were 14 males and 16 females. There were 17 white people and 13 Negro. Three persons were 0 to 2 years old; one was in the 2-to-10 year category; none were aged 11-20; 4, 21-30; 16, 31-40; 3, 41-50; 1, 51-60; and 2 were aged 61-70.

Place of Occurrence.—Six deaths occurred in the home, 12 at physicians' offices; 2 patients reacted at home and died at the time of arrival or soon after arrival at the hospital, and 3 reacted at physicians' offices and died shortly thereafter at the hospital. Seven deaths occurred at hospitals, these deaths being subdivided as follows: two patients were hospital employees treated at the employees' clinic, two died in an emergency room, one was a nurse treated by another nurse at the victim's request, and two were hospital patients (one of these being treated for a plantar ulcer in a case of peripheral vascular disease, the other receiving prophylactic therapy after an intranasal operation).

Time of Occurrence.—Twenty-five cases were of the immediate type, and five patients suffered delayed reactions. The time of the delayed reaction was 30 minutes for two patients, 20 minutes for one patient, 2 hours for one patient, and 14 days for one.

Dosage.—The amount of penicillin used was anywhere from 200,000 to 500,000 units. In two instances 20 mg. of chlorpheniramine (Chlor-Trimeton) maleate was administered in the injections; in one case 2 cc. (equivalent to 10 mg.) of a diphenhydramine (Benadryl) hydrochloride ampul was given simultaneously. These last three cases are the result of the warnings given by the drug houses, namely, that it is less risky, when there is doubt, to use simultaneously a dose of an antihistamine. This advice could have been misleading, since when protection against anaphylaxis is needed, the action of the simultaneously administered antihistamines could never be fast enough to save life. That the antihistamines might minimize a less catastrophic reaction might very well be, but they probably never prevented a death. Within the past few months a penicillinase preparation [10] has been made available which can be administered when a reaction is noted to be beginning, but even here the manufacturer admits its limitations in the type of event which occurred in 25 of the 30 cases. It is recommended by the manufacturer that this preparation be kept as handy as epinephrine and that it may even be used intravenously followed by another dose (800,000 units per dose) given intramuscularly almost simultaneously. The manufacturer should be complimented for being very clear in his instructions since he does state: "NOTE: In the rare acute anaphylactic reactions that cause patients to expire in minutes Neutrapen would not have time to be effective."

History.—In 14 cases no inquiry at all was made as to prior administration of and/or reaction to penicillin. In three cases the patients exhibited asthmatic symptoms which should have put the physician on guard in the use of penicillin, since reactions may be more apt to occur to penicillin in patients with a history of asthma. In only one instance do we have complete authenticated evidence of a direct inquiry having been made and a negative answer obtained. With reference to three persons known to have reacted previously, the physicians stated that they had made inquiry and received negative replies but the reverse was alleged by the patients' families. In only 7 cases are we absolutely certain of a prior known sensitivity, and in 12 cases we could not obtain an authenticated history of a prior reaction. From all this it is obvious that one is hard pressed in making a survey of this type to get the crucial information because of the subsequent possibility of a legal problem.

Indications for Use of Penicillin.—The part of the study concerning indications for the use of penicillin necessarily requires sincere objectivity, albeit there was arbitrariness on our part. Thus,

the cases have been divided into 12 in which it is felt the use of penicillin was indicated (omitting for the moment the matter of inquiry about previous use and reaction or lack of it), 13 cases in which the indication for the use of the drug was questionable, and 5 cases in which we thought it was not indicated. The diagnoses for which the drug was given are enumerated and have been arbitrarily divided as to indications as follows: The use of the drug was indicated for upper respiratory infection with fever in 4 patients; for venereal disease in 5; for erysipelas in 1; for peridental abscess in 1; and for plantar ulcer in 1; for a total of 12. Indications for use of the drug were questionable for upper respiratory infection without fever in 12 and for paronychia in 1, for a total of 13. The drug was not indicated for nonspecific skin eruption in one, for sprained toe in one, for injury to a finger in one, for stasis dermatitis in one, and for postoperative intranasal surgery in one, for a total of five.

Legal Aspects

Nine cases of fatal reaction to penicillin are or have been the subject of lawsuits as far as we can determine from our files. On this latter point a careful search was made of the New York County Lawyers Association Library. Inquiry was also made of the National Association of Claimant's Compensation Attorneys executive office and from a few prominent New York attorneys, even those associated with the malpractice claims against the doctors of New York State, about their knowledge of any court rulings on any similar cases. None recalled any. However, it is not unlikely that whatever claims were made either were settled just before they reached court or, having been tried, were not appealed. We know of one instance where the physician made a cash settlement because he did not carry malpractice insurance.

In going over the legal aspects of this problem, the following paragraph in Warren's "Negligence in the New York Courts" was noted: [11]

> To a large extent, at least, the knowledge and skill required of a physician or surgeon depends upon the state of the profession. . . . he is required to have the knowledge and skill of the average member of his profession in good standing in the community in which he is practicing. This means, of course, that he is not required to anticipate future discoveries. It is an elementary proposition that the medical profession advances in knowledge as time goes on. New discoveries are constantly being made. As a result of this, at the time of a trial of an action such new discoveries may have rendered improper a course of treatment previously followed. If, however, this treatment, at the time it was given, followed that generally used by members of the medical profession at that time, it will free the physician from liability.

The above paragraph is self-explanatory. Insofar as the penicillin problem is concerned, there is no longer any doubt as to the ability of this drug to cause fatal reactions, nor can it be denied that by now such possibility should be known to all who use it.

But even the greatest care in inquiring about any previous use of penicillin and/or reactions thereto may fail to reveal unknown sensitization. Two facts have shed some light on the possible means of such sensitization. One concerns the innocent ingestion of penicillin through the drinking of milk, and the second concerns penicillin formation and its absorption from skin where it was made by pathogenic fungi. As to the milk problem, reports in *Veterinary Medicine* [12] state that 5.9% to 11.6% of the milk reaching the consumer contains penicillin in concentrations ranging from 2 to 80 units per glass.[13] The penicillin had been injected by the farmer into the cow's udder for the control of mastitis, which cleared in a day or so, making that cow's milk marketable, but it takes about four days before all the penicillin disappears from the udder. Warnings on labels not to market the milk for at least 72 hours are often completely disregarded. Thus, the patient may unknowingly become sensitized to penicillin. The second means of unsuspected sensitization was shown many years ago by Peck and Hewitt [14] and recently by some Hungarian investigators who noted that pathogenic fungi living on the human skin could, in some instances, produce penicillin. The latter could then be absorbed and in time sensitize the individual to penicillin and thus be the basis for a later reaction to the drug when used therapeutically.

Therefore, it is now apparent that the physician is faced with a true dilemma, since even the most careful and complete questioning of a patient may give him no warning about a subsequent reaction. Most people drink milk, and not a few have or have had some form of epidermophytosis. It seems reasonable, in the light of the above work, to avoid the use of penicillin in people with a history of "athlete's foot." In order to illustrate more vividly the problem of fatal penicillin reactions, a few selected cases are described.

Report of Cases

Case 1.—A 38-year-old female was under treatment by her physician for syphilis. She had had two prior injections of penicillin of 600,000 units each, the last one about a month before the present one. At this visit, the physician stated to the medical examiner that he had made an inquiry about any previous reaction and had received a negative reply. He then injected 600,000 units of procaine penicillin intramuscularly into the buttock. Within a few moments the patient complained of feeling dizzy, collapsed, and, despite the injections of epinephrine and coramine, she died. While the details of the story were being obtained from the doctor at his office, the scene of the death, the patient's husband appeared, having been notified of the death by the physician and the police. The husband was questioned about his wife and it was learned from him that after the previous injection about a month before, his wife had developed "bumps" all over her body and was sick for about 12 days thereafter. He further stated that they had called the physician to notify him of this occurrence. The doctor denied any knowledge of this information. The vial from which the drug was drawn was checked by our chemists and identified as procaine penicillin and was not outdated. A complete autopsy was performed, and other than

old tuberculous peritonitis, nothing was found but visceral congestion. The injection site revealed that the penicillin crystals had not entered any blood vessel. Microscopy was negative except for visceral congestion and tuberculous peritonitis.

CASE 2.—A 40-year-old female was being treated at her physician's office for a "sprained toe." She was given 300,000 units of procaine penicillin intramuscularly, and, while receiving some physiotherapy to her toe, she began to feel weak, complained of respiratory distress, collapsed, and was pronounced dead about a half hour later despite the use of stimulants. Inquiry by the medical examiner of the doctor as to any previous reaction yielded a negative answer. However, the husband of the deceased told the medical examiner that about three months before his wife had had a "bad reaction" after an injection of penicillin for a "sore throat." A complete autopsy was entirely negative. Even a dissection of the "sprained toe" failed to reveal any local tissue changes. Microscopy was negative except for visceral congestion.

CASE 3.—A 33-year-old female was seen at her physician's office for the treatment of a paronychia of the left thumb. The doctor stated that he had made inquiry of the patient about previous use of penicillin and learned that she had received penicillin before but had not had any untoward reaction after its use. He then administered 300,000 units of procaine penicillin intramuscularly. The patient left the office but returned a few minutes later stating that she was not feeling well, and she was noted to be in respiratory distress. The doctor placed her on the waiting room floor, gave her an injection of epinephrine, and called for an ambulance. She was admitted to the hospital in coma and died about an hour later despite all measures taken to revive her. Dr. Helpern performed this autopsy and reported pulmonary congestion, some laryngeal edema with encroachment on the aperture of the larynx, abundant viscid mucoid secretions in the trachea, and a paronychia on the radial side of the left thumb.

CASE 4.—A 31-year-old male reported to his physician's office, complaining of a sore throat. The doctor examined him and found that the patient had a "red throat" and fever. The physician suggested that the patient be hospitalized, but this was refused. The patient was then given 600,000 units of procaine penicillin intramuscularly. The patient went home and prepared for bed while his wife went out to fill a prescription. Upon her return, he was dead. The medical examiner investigating the case was told by the physician that inquiry had been made about prior penicillin administration to which an affirmative answer was obtained and that the patient had made no mention of any reaction to the drug. However, the patient's wife told the medical examiner that about a year before this he had received penicillin for some minor ailment after which he had angioneurotic edema. A complete autopsy revealed pulmonary edema and congestion and some laryngeal edema.

In all the above cases complete chemical examinations of the viscera were made by the toxicological laboratory of the Office of Chief Medical Examiner with negative findings. Microscopically only intense visceral congestion was noted except where pneumonitis was found and in those cases it was postulated ante mortem.

Summary

A statistical survey of 30 authenticated fatal anaphylactic reactions to penicillin, recorded in the files of the Office of Chief Medical Examiner of the City of New York, has many implications. There is the possibility of unknown sensitization to penicillin by means of the ingestion of penicillin-containing milk and its products or by absorption through the skin from dermatophytes, thus paving the way for a later unpredictable reaction to the therapeutic use of the drug. Careful inquiry regarding the patient's allergic reactions in the past should precede the administration of penicillin. Such safety measures are important for their legal implications as well as for the sake of the patients.

The author wishes to express his appreciation to Dr. Milton Helpern and the entire Medical Examiner Staff for their kind assistance in the preparation of this material.

References

1. Rosenthal, A.: Eight Fatal Anaphylactic Reactions to Penicillin, New York J. Med. **54**:1485-1487 (May 15) 1954.

2. Curphey, T. J.: Fatal Anaphylaxis in Bronchial Asthma Following Administration of Penicillin, New York J. Med. **53**:1107-1110 (May 1) 1953.

3. Corr, D. J., and Wellman, W. E.: Reactions to Penicillin: I. Review of Literature Concerning Severe Reactions (English and North American), Minnesota Med. **39**:599-610 (Sept.) 1956. Lewis, G. W.: Acute Immediate Reactions to Penicillin, Brit. M. J. **1**:1153-1157 (May 18) 1957.

4. Welch, H.; Lewis, C. N.; Weinstein, H. I.; and Boeckman, B. B.: Severe Reactions to Antibiotics: Nationwide Survey, Antibiotic Med. **4**:800-813 (Dec.) 1957.

5. Bell, R. C.: Anaphylactic Shock due to Oral Penicillin, Lancet **2**:439-441 (Sept. 1) 1956. Weiner, R. G.; Necheles, J. R.; and Stanka, H.: Anaphylaxis Following Oral Administration of Penicillin, Am. Pract. & Digest Treat. **7**:377-380 (March) 1956. Manganzini, H. C.: Anaphylactoid Reaction to Penicillins V and G Administered Orally: Report of Two Cases and Brief Review of Subject, New England J. Med. **256**:52-56 (Jan. 10) 1957. Eisenstadter, D., and Hussar, A. E.: Severe Anaphylactic Reaction from Oral Penicillin, Am. Pract. & Digest Treat. **5**:783-784 (Oct.) 1954. Madalin, H. E.: Anaphylactoid Reaction Following Use of Penicillin Lozenge, J. Michigan M. Soc. **53**:61, 91 (Jan.) 1954. Mason, L. H.: Case of Fatal Shock Following Oral Penicillin, Canad. M. A. J. **76**:958-959 (June 1) 1957. Gullatti, R.: Brief Recording: Anaphylactic Shock from Penicillin Lozenge, New England J. Med. **257**:1037 (Nov. 21) 1957.

6. Smith, V. M.: Fatal Reactions to Penicillin: Evaluation of Test for Sensitivity, New England J. Med. **257**:447-451 (Sept. 5) 1957.

7. McCuiston, C. F.: Penicillin-Sensitivity Test, Correspondence, New England J. Med. **257**:1144 (Dec. 5) 1957.

8. Kern, R. A., and Wimberley, N. A., Jr.: Penicillin Reactions: Their Nature, Growing Importance, Recognition, Management, and Prevention, Am. J. M. Sc. **226**:357-375 (Oct.) 1953.

9. Siegal, S.: Fundamentals of Modern Allergy: Allergy to Penicillin, New York J. Med. **58**:2859-2862 (Sept. 15) 1956.

10. Minno, A. M., and Davis, G. M.: Penicillinase in Treatment of Penicillin Reactions, J. A. M. A. **165**:222-224 (Sept. 21) 1957.

11. Warren, O. L.: Negligence in New York Courts, ed. 2, New York, Matthew Bender & Co., 1950, p. 102, paragraph C.

12. Penicillin in Fluid Milk, Editorial Comments, Vet. Med. **52**:95 (Feb.) 1957.

13. Long, P.: Personal communication to the author.

14. Peck, S. M., and Siegal, S.: Successful Desensitization in Penicillin Sensitivity, J. A. M. A. **134**:1546-1547 (Aug. 30) 1947. Peck, S. M., and Hewitt, W. L.: Production of Antibiotic Substance Similar to Penicillin by Pathogenic Fungi (Dermatophytes), Pub. Health Rep. **60**:148-153 (Feb. 9) 1945. Uri, J.; Szathmary, S.; and Herpay, Z.: Production of Antibiotic by Dermatophytes Living in Horn Products, Nature, London **179**:1029-1030 (May 18) 1957.

THE JOURNAL
OF THE AMERICAN MEDICAL ASSOCIATION
Edited Under the Direction of the Board of Trustees

Editor and Managing Publisher . AUSTIN SMITH, M.D.
Associate Editor . . . . . JOHNSON F. HAMMOND, M.D.
Assistant Editors . . . . . WAYNE G. BRANDSTADT, M.D.
FREDERIC T. JUNG, M.D.
EDWARD R. PINCKNEY, M.D.
Assistant to the Editor . . . . . MILTON GOLIN
Editor for Medical Literature Abstracts . GEORGE HALPERIN, M.D.
News Editor . . . . . CHARLES CHAPMAN

Subscription price . Fifteen dollars per annum in advance
Cable Address . . . . . "Medic, Chicago"

PERINATAL MORTALITY AND MORBIDITY PROGRAMS IN THE UNITED STATES

THE PROBLEMS of perinatal mortality and morbidity are currently more prominent than those of maternal mortality. The latter have been attacked vigorously for some time, and where this has been done the lowering of maternal mortality rates has, on the whole, reduced perinatal deaths as well. In other words, good maternal health is associated with healthy newborn infants. Nevertheless, these efforts have not been enough. The large number of early infant (neonatal) deaths has long deterred many committees and medical study groups from attempting any sort of comprehensive mortality analysis such as has become relatively common for maternal deaths. The time has come, however, when more concerted effort must be directed toward problems more specifically related to the reduction of perinatal mortality and morbidity.

Recent national statistics show a continuous and significant decrease in maternal deaths, whereas the rate of decrease of neonatal deaths is proportionately much less. This is in spite of the fact that the "irreducible minimum" in maternal mortality was thought by some to have been reached several years ago. The maternal mortality rate for 1956 was 3.8 deaths per 10,000 live births, as estimated by the national office of Vital Statistics.[1] This is a 76% reduction during the 10 years since 1946. In contrast to this is the relatively low reduction in neonatal deaths, only 22% during the same period. The total number of infant deaths registered in the United States in 1956 was 108,300 (26 per 1,000 live births), of which 78,160 (72%) were during the first 28 days (the neonatal period).

"Perinatal" is a relatively new term already widely used by many workers in this field. In many instances it is used to include neonatal deaths and late and intermediate fetal deaths. However, inclusions used in calculating the perinatal mortality rate vary from one place to another with respect to the maximum length of time after birth and the minimum number of weeks of gestation. The number of fetal deaths reported approximates that of neonatal deaths, but because of the varying degrees of completeness in the reporting of fetal deaths, the total number is not accurately known. For this reason rates are often based upon total live births rather than total births.

The Committee on Maternal and Child Care is studying these problems of the perinatal period (neonatal and fetal) and the current efforts to solve them. In cooperation with other interested persons and groups, the Committee is working toward the development of a study guide on this subject for state and local medical societies, health departments, and hospitals as an appropriate sequel to the guide for maternal death studies.[2] It is believed that wide use of such material will expedite the prevention of avoidable deaths and will stimulate interest in efforts to further reduce both maternal and perinatal mortality and morbidity.

The first report in this series by the Committee (see under Council on Medical Service, page 1124, this issue) will describe the pioneering work of the Philadelphia group in its study of neonatal mortality. The experiences of medical groups in other areas will be described in succeeding reports. The Committee's purpose in publishing these articles is to help acquaint the medical profession with what is being done in various areas. The methods and results of these many local and state programs will be studied and compared, and the techniques that are considered most effective will be incorporated into the study guide. Regional meetings have been held for discussion and agreement on many points involved. Other meetings are planned in order to collate findings; and additional regional meetings are anticipated as a means to disseminate information and stimulate interest in further efforts to lower perinatal mortality and morbidity.

1. Annual Summary for 1956, part 2, Estimated Numbers of Deaths and Death Rates for Selected Causes: United States, 1956, Vital Statistics Monthly Reports 5:13 (May 10) 1957.

2. Guide For Maternal Death Studies with Causes of Obstetric Deaths, Direct and Indirect, and Reports on Study of Seven Programs, Committee on Maternal and Child Care, Council on Medical Service, A. M. A., 1957.

ORGANIZATION SECTION

BLUE SHIELD AND EDUCATION

What are the effects of Blue Shield on graduate medical education? Dr. Edward L. Turner, Secretary of the Council on Medical Education and Hospitals, and Dr. Ward Darley, executive director of the Association of American Medical Colleges, attended a meeting, in Chicago, with representatives of Blue Shield several weeks ago when some problems that have been associated with the development of prepaid insurance were discussed in the light of graduate medical education. The conferees concluded that this area is deserving of cooperative study by the AAMC, the A. M. A. Council on Medical Service and Council on Medical Education and Hospitals, and other organizations which might be involved. "It is inevitable," said Dr. Turner, "that this general field involving prepayment will, as time goes by, become of increasing concern to medical education in all of its phases—as well as to medical care itself."

958
167

HOSPITAL MEDICAL EDUCATION

The feasibility of establishing a broad educational program for hospital directors of medical education was discussed recently at a meeting in Chicago. In attendance were representatives of the A. M. A. Council on Medical Education and Hospitals, the American Hospital Association, and the Association of Hospital Directors of Medical Education. The group recommended that, as a first step, 20 to 25 individuals experienced in the field of education gather together at an "invitational workshop" to study need, relationships, types of training, and directorial qualifications in hospital medical education programs. An advisory committee was to be established to work out further details.

MEETING ON WARNING ON CHEMICAL PRODUCTS

The Committee on Toxicology will conduct a meeting July 25 at A. M. A. headquarters, in Chicago, to discuss proposed legislation requiring the declaration of hazardous ingredients and warning statements on the label and in the accompanying literature of household, commercial, and industrial chemical products. Representatives of interested industries and trade associations also will attend. Further information may be secured from the Committee at A. M. A. headquarters.

FILMS OF THE SAN FRANCISCO MEETING

Filmed highlights of the 107th A. M. A. Annual Meeting—presented by the American Medical Association in cooperation with Merck, Sharp & Dohme—will be available after Sept. 1, for showing to medical meetings. Entitled "San Francisco—1958" (television abstracts of the A. M. A. Annual Meeting), the 40-min. black and white films taken from kinescopes of five daily television programs may be secured from either the A. M. A. Film Library or Merck, Sharp & Dohme, Philadelphia. These programs will feature interviews with speakers on the convention program.

EXHIBIT ON FITNESS

"Seven Paths to Fitness" is the title of a new A. M. A. exhibit to be shown first at the Public Relations Institute, Aug. 27-28, in Chicago. Sponsored by the Bureau of Health Education in cooperation with the Bureau of Exhibits, the display emphasizes the seven avenues to health and fitness: nutrition, relaxation, play, exercise, dental care, medical care, and work. Over-all murals depict the sources and activities in each category. The exhibit is primarily intended for professional audiences having a direct interest in physical fitness. It will be available for bookings after Sept. 1, through the Bureau of Exhibits. A smaller type exhibit on the same subject will be completed later.

CHANGE OF ADDRESS

If you change your address please notify THE JOURNAL at least six weeks before the change is made. Include the address label clipped from your latest copy of THE JOURNAL, being sure to clearly state both your old and new address. If your city has Postal Zone Numbers, be sure to include this Zone Number in your new address.

MEDICAL EDUCATION IN PUERTO RICO

A recent survey of intern and residency training programs in Puerto Rico indicates the carrying out of good teaching programs and an intense interest and enthusiasm to teach on the part of attending staffs. Dr. Arthur N. Springall, Assistant Secretary of the A. M. A. Council on Medical Education and Hospitals, reported on a study of a total of 17 facilities—including government hospitals, the medical school of the University of Puerto Rico, the Veterans Administration Hospital, and some private institutions on the island. He found that medical records in Puerto Rico hospitals compare favorably with those of teaching hospitals on the continent, that there is considerable interest in multiphasic rehabilitation of patients, and that there is a wealth of clinical material available for study. There also is a need for pathologists on the island. A new medical center is being planned for San Juan, with construction of one new unit expected to begin in a few weeks. Dr. Springall reported that a majority of house staffs are native Puerto Ricans graduated from Spanish and Mexican medical schools.

COUNCIL ON MEDICAL SERVICE

STUDY OF PERINATAL MORTALITY AND MORBIDITY PROGRAMS IN THE UNITED STATES

PART 1
PHILADELPHIA NEONATAL MORTALITY STUDY

Closely related to the study of maternal deaths in Philadelphia, which began in 1930, was a study of neonatal deaths. The latter was initiated in 1931 by a subcommittee of the Maternal Mortality Committee of the Philadelphia County Medical Society in cooperation with the Philadelphia Department of Public Health.

Because of a shortage of personnel during World War II and the departure of certain key individuals, the study lapsed in activity. However, at the request of the Philadelphia County Medical Society, a Philadelphia Neonatal Study Committee was established in 1946, with members representing the medical schools and hospitals of Philadelphia. Later this committee was reorganized into one of the active coordinating committees of the medical society in cooperation with the local obstetric and pediatric societies. Its purpose in studying the problems of the neonatal period is to discover the causes of neonatal deaths and the preventable factors involved, to reduce thereby the number of such deaths, and to further understanding of the causes of prematurity.

The membership of the committee consists of a representative from the pediatric department of each of the 48 hospitals. Its chairman is appointed by the president of the county medical society upon the recommendation of the local pediatric society. It is informally understood that each chairman, if he is willing, will serve for about 10 years to assure continuity of the programs. A steering committee of 12 is appointed from the members of the full committee by the president of the county medical society upon the recommendation of the chairman for staggered four-year terms. It has been the policy to include at least one representative from each of the five teaching institutions. The secretary of the Neonatal Study Committee is a staff member of the maternal and child health section of the Philadelphia Department of Public Health.

Scope of Study

All deaths in Philadelphia of infants less than 28 days old are included in the study. Matching of birth and death certificates, which was started in 1953, makes it possible for all neonatal deaths to be classified by the hospital of birth. The committee does not study morbidity as such, but topics discussed at open committee meetings have included management of erythroblastotic infants, fluid and electrolyte balance, early detection of congenital defects and preventable surgical procedures. As the need arises ad hoc subcommittees are appointed on such matters as prematurity and hospital nursery records.

This is the first of a series of articles prepared by the Committee on Maternal and Child Care of the Council on Medical Service on perinatal mortality and morbidity study programs that are being conducted in various parts of the United States. Subsequent articles will appear in THE JOURNAL from time to time.

Committee members are W. L. Crawford, M.D., Chairman, Rockford, Ill.; R. B. Chrisman Jr., M.D., Coral Gables, Fla.; Philip S. Barba, M.D., Philadelphia; Harold S. Morgan, M.D., Lincoln, Neb.; Garland D. Murphy, M.D., El Dorado, Ark.; Howard A. Nelson, M.D., Greenwood, Miss.; J. L. Reichert, M.D., Chicago; Donald A. Dukelow, M.D., Consultant, Chicago; and Mr. George W. Cooley, Secretary, and Mr. Donald B. Berg, Research Assistant, Chicago.

Method of Operation

Case-finding and Collection of Data.—Through the cooperation of state and local health departments, transcripts of the neonatal death certificates for Philadelphia are sent to the committee secretary's office in the maternal and child health section. Prior to July 1, 1955, the secretary's office would send a study form to the hospital where a neonatal death occurred, with the request that it be filled out by the committee hospital representative or a person designated by him and returned as promptly as possible. This voluntary reporting rose from 60% in the earlier years of the study to almost 95% in 1955. Since July 1, 1955, a supply of study forms has been regularly sent to each hospital representative. The forms are filled out by the attending physician and the residents, interns, and other hospital personnel acquainted with the particular neonatal death and are submitted to the hospital representative for review and forwarding to the committee secretary. Periodically, each hospital representative is sent a list of the neonatal deaths for which completed forms have not yet been received. Also, individual physicians known to be familiar with the case are requested to supply pertinent information which may not be available from the hospital records. Standardized forms are also used for these contacts.

958
167

Processing of Data.—Until recently the steering committee reviewed each case individually, decided the cause of death, and determined the rating of responsibility. Since these deaths number about 1,200 annually, several specially trained physicians of the maternal and child health section of the department of public health now screen the study forms, leaving only unusual or controversial cases to be decided by the steering committee. These physicians code the data which is subsequently transferred to punch cards for statistical analysis. Anonymity is assured; the hospital representative, the committee secretary, and the physician who codes the questionnaire are the only persons who know the names appearing on the study form except in cases discussed by the whole steering committee. These study forms are kept on file in the health department as privileged and confidential material.

As may be seen from the foregoing, close working relationships are maintained between the Philadelphia County Medical Society, the Philadelphia Department of Public Health, the Philadelphia Pediatric Society, and the Obstetrical Society of Philadelphia. This cooperation extends to the financing and use of facilities. Space is provided at both the County medical society building and the department of public health for a secretary who functions in both offices. Meeting rooms are provided by the medical society, which also furnishes office supplies and equipment, postage, etc. The medical society has shared the expense of sending a representative to national and other meetings, and it has also shared the cost of exhibits. The department of public health in turn supplies staff for preparation of reports, provides the services of a statistical consultant (on a limited basis), supplies report forms and tabulation cards, secures and distributes reprints, manuals, and books, and pays the costs of mailing meeting notices and other material as well as general administrative and clerical costs.

The steering committee meets about three or four times a year to set policies, develop programs, and review selected unusual or controversial neonatal deaths. At these meetings preparations are made for the regular bimonthly open luncheon meetings of the full committee. All hospital representatives are sent invitations and, in addition, notices inviting interested physicians, nurses, medical students, interns, and residents are sent to each hospital for posting. Attendance ranges from 30 to 50. At these bimonthly meetings one or more cases are presented to illustrate such particular topics as pulmonary hyaline membrane, management of the small premature infants, or Rh incompatibility. Bimonthly joint open meetings are also held with the Maternal Welfare and Fetal Death committees for discussion of neonatal deaths with obstetric implications. These joint meetings also discuss the rating of responsibility. All neonatal deaths are classified according to the International Statistical Classification of Diseases, Injuries, and Cause of Death [1] and are rated as probably preventable, nonpreventable, or unclassifiable. Where deaths are rated as probably preventable they are classified as antenatal (obstetric), postnatal (pediatric), or combined and are assigned more specifically to (1) inadequate prenatal care, (2) the fault of the family, (3) physician's error in judgment, (4) physician's error in technique, (5) intercurrent disease, and (6) unavoidable disaster.

Follow-up and Use of Findings.—A yearly report of neonatal mortality (by hospital) is sent to each hospital's administrator, medical superintendent, president of the board of trustees, chairman of the staff, head of the obstetric department, head of the pediatric department, head of nurses, chief obstetric nurse, and the hospital representative on the Neonatal Study Committee. Hospital names are omitted except for that of the hospital receiving the report; the listing is, rather, by numbers of live births. Also given are the number of neonatal deaths and the rate (with standard deviation) per 1,000 live births. Administrators of hospitals with rates higher than the city's average receive a personal follow-up letter from the health commissioner, with copies sent also to the heads of obstetrics and pediatrics. This letter, which

points out that no criticism is intended, indicates the willingness of the health department through its maternal and child health section to arrange meetings of consultants with personnel of the hospital to help solve any problems regarding neonatal mortality and morbidity. Replies to these letters have been appreciative, and several hospitals have asked for conferences.

Reports to the profession are published in the county medical society's journal at frequent intervals and also in state and national journals. Reports to the public on the activities of the committee appear from time to time in newspaper editorials and articles. The hospital council also publicizes committee activities through its newsletter. Hospital staff members are urged to discuss each neonatal death at their regular meetings. The committee's findings are also used for teaching purposes in the five local medical schools.

A review committee has been established consisting of the chairman of each of the three mortality study committees, a representative of the department of public health, and a representative of the hospital association. The purpose is to coordinate activities, review policies, and look for ways and means to improve the effectiveness of their study programs.

TABLE 1.—*Neonatal Deaths and Death Rates, Philadelphia, Selected Years, 1940-1956**

Year	Live Births, No.	Neonatal Deaths, No.	Deaths/1,000 Live Births
1940	31,227	846	27.1
1945	38,825	976	25.1
1950	47,516	1,058	22.1
1951	50,318	1,054	20.9
1952	51,661	1,113	21.5
1953	51,706	1,162	22.5
1954	53,716	1,252	23.3
1955	52,368	1,305	24.9
1956	53,203	1,236	23.2

* Data supplied by the office of Statistics and Research, Philadelphia Department of Public Health.

Results

The statistical data in the following paragraphs are from the office of statistics and research of the Philadelphia Department of Public Health.

Analysis of the 1953 statistics revealed that about 70% of the neonatal deaths were in premature infants (2,500 Gm. or less). Ninety per cent occurred during the first week and over 50% on the first day. In individual hospitals the neonatal death rates ranged from 8.4 to 44.6 per 1,000 live births.

Table 2, which presents the causes of neonatal death in Philadelphia in 1953, shows that the category "injury at birth" accounts for over one-fourth of the total. This category (injury at birth, 760-761, in the International Classification) includes many more clinical diagnoses and obstetric situations than clinicians are usually aware. The term is apt to be associated only with such iatrogenic factors as intracranial hemorrhage following prolonged labor or application of high forceps. Also in this category, however, are compression, prolapse, knot or strangulation of the umbilical cord; placenta previa; precipitate birth; abnormal presentation (breech, foot, tranverse, etc.); version; and such conditions as edema of the brain.

TABLE 2.—*Causes of 1,162 Neonatal Deaths, Philadelphia, 1953*

Causes*	Premature † No.	Premature † %	Full-term ‡ No.	Full-term ‡ %	Birth Weight Unknown No.	Total No.	Total %
Postnatal asphyxia and atelectasis (762)	185	22.6	38	11.8	7	230	19.8
Injury at birth (760,761)	208	25.5	98	30.6	4	310	26.7
Congenital malformation (750-759)	48	5.9	80	24.9	1	129	11.1
Infection of newborn infant (763-768)	55	6.7	41	12.8	0	96	8.2
Blood dyscrasias (770,771)	16	2.0	25	7.8	2	43	3.7
Prematurity (774,776)	244	29.9	3	0.9	5	252	21.7
All other known causes (769,772,773)	39	4.8	24	7.5	2	65	5.6
Unknown cause	21	2.6	12	3.7	4	37	3.2
Total	816	100.0	321	100.0	25	1,162	100.0

*According to International Statistical Classification of Diseases, Injuries, and Causes of Death (6th revision), with International Classification number given in parentheses.
† 2,500 Gm. or less.
‡ More than 2,500 Gm.

Prematurity (mostly unqualified) is the second highest cause (21.7%) of neonatal death, with postnatal asphyxia and atelectasis ranking third (19.8%) (table 2). It should especially be noted that 30.6% of the neonatal deaths in full-term infants were due to birth injury, as were 25.5% of the deaths in infants. Also of special interest is the fact that postnatal asphyxia and atelectasis caused twice as many neonatal deaths among premature as among full-term infants.

TABLE 3.—*Survival of Premature Infants, Philadelphia, 1953*

Birth Weight, Gm.	Live Births, No.	Neonatal Deaths, No.	Survival, %
1,000 or less	325	325	0.0
1,001-1,500	397	210	47.1
1,501-2,000	860	166	80.7
2,001-2,500	2,896	115	96.0
Total	4,478	816	81.8

No premature infants weighing under 1,000 Gm. survived the neonatal period (table 3), and the over-all premature neonatal mortality was 18.2%. Table 4 shows the wide range between the neonatal mortality rate in the weight groups and the total rates for neonatal deaths in whites and nonwhites.

It should be noted that the 23.1% nonwhite births in 1953 accounted for 35.4% of the neonatal deaths. (Analysis of 1954 and 1955 data will soon be available.)

Comments and Conclusions

The Neonatal Study Committee, through its detailed study and analysis of neonatal deaths in cooperation with the Philadelphia Department of Public Health, has been able to define specific problems and is now initiating programs to solve them. Steps are being taken to assure more adequate prenatal care as one means of reducing the number of prematurely born infants; it is in this group (8.7% of all live births in 1953) that 70% of the neonatal deaths occur. The committee, in cooperation with the department of public health, is working to establish better facilities for care of premature infants in the larger hospitals, reception centers for such infants in strategic locations throughout the city, in-training courses for nurses, and a center to provide training for hospital teams of physicians and nurses in modern methods of caring for premature infants.

TABLE 4.—*Neonatal Mortality, Premature and Full-term, Philadelphia, 1953*

Birth Weight	No. of Live Births	No. of Neonatal Deaths	Deaths/1,000 Live Births
1,000 Gm. or less	325	325	1,000.0
2,500 Gm. or less	4,478 (8.7%)	816	182.2
2,501 Gm. or more	47,206	321	6.8
Unknown	25	25	1,000.0
Total	51,706	1,162	22.5
White	39,725 (76.9%)	751	18.9
Nonwhite	11,981 (23.1%)	411	34.3

The committee recommends that each hospital survey its nursery facilities and procedures and make whatever changes and improvements are necessary to conform with the Standards and Recommendations for Hospital Care of Newborn Infants, published by the American Academy of Pediatrics.[2] It also recommends that each hospital make every effort to determine the exact cause of each death through autopsy performed by a pathologist well acquainted with pathological conditions in newborn infants. The committee urges that each hospital discuss its neonatal deaths at meetings attended by the staff obstetricians, pediatricians, pathologists, and nursing personnel and that such meetings classify each case as to responsibility and preventability. The maternal and child health section of the department of public health has expert, experienced obstetricians and pediatricians available for consultation to assist hospitals with their improvement programs. The committee seeks the active cooperation of all concerned to achieve its goal—the reduction of neonatal deaths by determining true causes and the possible avoidable factors involved.

Emphasis in the Philadelphia neonatal study has been chiefly on professional education through free discussion and general reports to physicians and hospital administrators. The effectiveness of this program is suggested by the growing local interest and participation in the study. In 1955, 94.6% of the 1,252 neonatal deaths were voluntarily reported. Several large neighboring hospitals outside the official health juridiction have asked to participate, and others have indicated their interest.

References

1. Manual of The International Statistical Classification of Diseases, Injuries, and Causes of Death, Sixth Revision of the International Lists of Diseases and Causes of Death, World Health Organization, Geneva, Switzerland, vol. 1, 1948, pp. 212-218.

2. Standards and Recommendations For Hospital Care of Newborn Infants, Full-term and Premature, American Academy of Pediatrics, 1954, revised 1957.

COUNCIL ON MEDICAL EDUCATION AND HOSPITALS

APPOINTMENT OF ASSOCIATE SECRETARY

The Council on Medical Education and Hospitals has announced the appointment of Dr. John C. Nunemaker as Associate Secretary of the Council as of Aug. 1. Dr. Nunemaker will be in charge of the graduate education aspects of the work of the Council dealing with internships and residencies.

Dr. Nunemaker, a native of Colorado, after receiving an M.D. from Harvard University in 1937, was on the house staff at Peter Bent Brigham Hospital in Boston and later an Assistant in Medicine at John Hopkins University. He served four years in the Army, having been Commanding Officer of a Station Hospital in Cairo, Egypt, and Surgeon of the Middle East Service Command. After this, he became Chief of the Medical Service, Veterans Administration Hospital, Salt Lake City, and Assistant Professor of Medicine, University of Utah College of Medicine. He went to Washington, D. C., in 1952, to head the Veterans Administration Research Service, after which he was appointed Director of Education and Service. Dr. Nunemaker is a Diplomate of the American Board of Internal Medicine and a member of the Government's Interdepartmental Committee on Scientific Research and Development.

MEDICAL NEWS

CALIFORNIA

Gift for Memorial Laboratories at Stanford.—Establishment of the William A. Ross Memorial Laboratories in the Medical Center under construction on the Stanford University campus after an initial gift of $100,000 from Mr. Ross' widow, has been announced. Initially the laboratories will be devoted to heart research. They will be constructed in the department of medicine, headed by Dr. David A. Rytand, in the clinic building, one of five buildings in the first stage of Stanford Medical Center construction. Mr. Ross, who was president of Columbia Steel Company, died in 1949.

Society News.—The California Society of Plastic Surgeons has elected the following officers: president, Dr. Gerald H. Gray, Oakland; vice-president, Dr. George V. Webster, Pasadena; historian, Dr. James B. Johnson, Beverly Hills; and secretary-treasurer, Dr. Richard A. Shepard, Oakland.—East Bay Psychiatric Association officers for 1958 are as follows: Dr. William M. McGaughey, Oakland, president; Dr. Richard L. Sutherland, Oakland, president-elect; Dr. Alan S. Mariner, San Leandro, secretary; Dr. Frederick R. Ford, Berkeley, treasurer.

CONNECTICUT

Dr. Kirchner Receives Mosher Award.—Dr. John A. Kirchner, associate professor of otolaryngology, Yale School of Medicine, New Haven, has received the annual Harris P. Mosher award in recognition of his work with the cricopharyngeus and its connection to the nervous system. This award is given by the American Laryngological, Rhinological, and Otological Society.

Personal.—Dr. Allan J. Ryan, Meriden, has been named literary editor of the *Connecticut State Medical Journal* by the council of the State Medical Society, to succeed Dr. Harold M. Marvin, New Haven, who resigned.—Dr. Louis P. Hastings, Hartford, has been reappointed to the Connecticut Medical Examining Board by Governor Ribicoff following recommendation by the State Medical Society. Dr. Hastings has served on the board for 10 years. He is full-time pathologist at St. Francis Hospital, Hartford.

Physicians are invited to send to this department items of news of general interest, for example, those relating to society activities, new hospitals, education, and public health. Programs should be received at least three weeks before the date of meeting.

Hospital News.—Renovation of the outpatient department of the Hospital of St. Raphael, New Haven, has been completed, and a formal opening for the public was held May 16. The 26-clinic department has new floors, ceilings, lighting fixtures, and structural changes to enlarge treatment, waiting, and interviewing space. Of the $158,000 spent for these improvements and equipment, $152,000 was a grant from the Ford Foundation. Other changes include air-conditioning of the hospital's surgical suite, enlargement of the surgical suite's recovery room, and renovation of the x-ray department, including equipment, totaling $130,000.

DISTRICT OF COLUMBIA

Appoint Chairman of Department of Medicine.—Dr. Lawrence H. Kyle, professor of medicine, Georgetown University School of Medicine, has been appointed chairman of the department of medicine, effective July 1, succeeding Dr. Hugh H. Hussey Jr., who will relinquish the post to become dean of the School of Medicine. Dr. Kyle joined the Georgetown faculty as a research fellow in endocrinology. In 1948 he was made William Wade Hinshaw Cancer Research Fellow and was appointed instructor in medicine. He has been director of the metabolic clinic of Georgetown University Hospital since 1943 and has been director of the metabolic laboratories since 1950. Dr. Kyle is a diplomate of the American Board of Internal Medicine (1951).

ILLINOIS

St. Francis Hospital Expansion Program.—St. Francis Hospital, Evanston, broke ground for a $5,630,000 expansion of the present building June 10. Construction of an extension along the front of the hospital and two extensions at the rear will provide 125 additional beds for patients and the enlargement of all departments. The outpatient department, emergency room, x-ray and laboratory sections will be relocated for easy access by patients. An expanded surgical pavilion will be included. The maternity division with newborn nurseries will be relocated and modernized and a large premature nursery provided. Funds for the expansion will be sought in a public campaign to be launched this fall. The public goal is $3,000,000. The Ford Foundation has given $230,100. The last addition to the hospital, now a 385-bed institution, was in 1928. The interns' residency was constructed in 1952. St. Francis was founded in 1900.

Chicago

Regulations for Reporting Blood Involvements.—In accordance with the recommendation of the Joint Maternal Welfare Committee of Cook County, the Chicago Board of Health has approved the following regulations:

It shall be the duty of every physician, laboratory, and hospital to report immediately to the Chicago Board of Health by telephone Rh negative mothers with a current pregnancy and to confirm it in writing within 24 hours.

It shall be the duty of every physician and hospital to report immediately to the Chicago Board of Health by telephone the birth of infants with hemolytic disease of the newborn and to confirm it in writing within 24 hours.

When confirming a report, physicians should write to the Chicago Board of Health, 54 W. Hubbard St., Hospital Audit Unit.

University News.—Prof. Etienne Wolff, of the Collège de France, Paris, presented "Growth of Human and Other Mammalian Cancers on Chick Embryo Organs in Vitro" and "Production of Monstrosities by X-rays and Their Prevention," the latter as a "George Shkoler Memorial Lecture," June 3 and 4, sponsored by the Mount Sinai Medical Research Foundation and The Chicago Medical School.——John P. Scott, Ph.D., chairman, Division of Behavior Studies at the Roscoe B. Jackson Memorial Laboratory, Bar Harbor, Maine, since 1945, joined the department of psychology in the Division of Biological Sciences of the University of Chicago April 1 as visiting professor for the quarter ending June 30.

958
167

INDIANA

Dr. Kohlstaedt Honored.—Dr. Kenneth G. Kohlstaedt, director of Eli Lilly and Company's clinical research division, Indianapolis, has received the first Certificate of Appreciation for Meritorious Service to be awarded by the American Academy of General Practice. The award was established by resolution of the A. A. G. P.'s Congress of Delegates at the 10th annual scientific assembly recently. Dr. Kohlstaedt was recommended for the award by the academy's Indiana chapter "in appreciation for the invaluable service . . . rendered the Academy for a number of years." He is an honorary member of the Indiana chapter.

Dr. Lilly Receives Pharmaceutical Medal.—Eli Lilly, LL.D., chairman of the board of directors of Eli Lilly and Company, has been selected by the past-presidents of the American Pharmaceutical Association to become the recipient of the 1958 Remington Honor Medal, established by the New York Branch of the association in 1918, "to be presented annually to the individual who has done most for American Pharmacy in the previous year, or whose continuing contributions to the advancement of the profession over a period of years have been most outstanding." In August, 1953, Dr. Lilly was elected honorary president of the association, which marked the first time the A. Ph. A. has given the honorary presidency to a father and son. Dr. Lilly's father was similarly honored in 1934.

KENTUCKY

Medical Scholarship Fund.—Twenty-eight students were added to the list of those receiving aid in financing their medical educations from the Rural Kentucky Medical Scholarship Fund at a recent meeting of its board of trustees, according to an announcement from Dr. Carl C. Howard, Glasgow, chairman of the board. Sponsored by the Kentucky State Medical Association, the fund is aimed at distributing adequate medical care to rural Kentuckians and helping worthy students interested in rural practice to gain a medical education. Since its inception in 1946, it has aided 137 students with 335 loans amounting to nearly $257,000. Currently 22 of the recipients are fulfilling their obligations to the fund by practicing in rural Kentucky areas, 14 are continuing their practice after fulfilling their obligations later, 13 are completing internships and residencies, and 47 are in medical schools. The board of trustees administers the fund, which in recent years has been aided by grants from the state legislature.

LOUISIANA

Dr. Paterson Named Department Chairman.—Dr. John C. S. Paterson, associate professor of medicine, Tulane University of Louisiana School of Medicine, New Orleans, will become chairman of the department of tropical medicine and public health July 1. Dr. Paterson is a native of Scotland. He came to the U. S. in 1949 to attend the University of Rochester in New York under a Commonwealth Fund fellowship. He returned to the University of London as tutor in medicine until he joined the faculty at Tulane in 1953. Dr. Paterson was awarded the M.D. degree with commendation in 1956 for his thesis on diurnal variations in the metabolism of iron. He has done research in sickle-cell disease, metabolism of iron, cerebral circulation, and epidemiology of leukemia. Dr. Paterson's wife, Dr. Ruth D. Paterson, assistant professor of neurology at Tulane, is also a member of the Royal College of Physicians, London.

Extend Consultant Services to South America.—Tulane University, New Orleans, has contracted with the International Cooperation Administration to extend its consultant services to the seven medical schools of Colombia, South America, for three more years. In 1955 at the request of the Colombia medical schools the project was begun to provide advice to the Colombian schools in making changes in the medical curriculum and to strengthen basic medical science teaching. Five Tulane consultants

have spent three months each in Colombia, and opportunities have been extended to Colombian physicians to come to the U. S. on fellowships for advance study. Partly as a result of this program, 22 Colombian students and faculty members have been in training at Tulane during the past year and others have been aided in getting support to study in medical centers throughout the country. Direct results of the program include the establishing of an enterobacteriological center in Cali and a cooperative research project to investigate the clinical significance of various tropical parasites.

MASSACHUSETTS

Dr. Lee and Professors Emeriti Honored.—Ceremonies honoring Dr. Roger I. Lee, first acting dean of the faculty of public health at Harvard University, Boston, and a past-president of the American Medical Association, and the professors emeriti of the School of Public Health were held May 28. Citations honoring Dr. Lee and each of 10 professors emeriti were presented by members of the faculty. In addition to Dr. Lee, the guests of honor included:

Dr. Alice Hamilton, Hadlyme, Conn., Dr. Frederick Fuller Russell, Louisville, Ky., Dr. Ernest Edward Tyzzer, Wakefield, Mass., Edwin Bidwell Wilson, Ph.D., Brookline, Dr. Richard Mason Smith, Boston, Dr. George Cheever Shattuck, Brookline, Melville Conley Whipple, Tamworth, N. H., Dr. Harold Coe Stuart, Chestnut Hill, Dr. Franz Goldman, New Rochelle, N. Y.

MICHIGAN

Dr. Neafie Honored.—Dr. Charles A. Neafie, for 40 years a health officer in Pontiac, received from the Michigan Health Officers Association May 8 a distinguished health service award. Dr. Neafie is a past-secretary and past-president of the Oakland County Medical Society and former member of the council of the Michigan State Medical Society. The Michigan Health Officers Association also made Dr. Neafie "president for a day" of the association.

Increase Enrollment at Wayne.—With legislative approval, Wayne State University's board of governors has voted to increase the College of Medicine enrollment from 75 to 125 freshmen students, beginning in September. Funds to cover expansion will come from the state's general appropriation to the university of $9,718,900. Estimated cost for the additional students is $285,000 for the first year. By 1962, the total medical school enrollment is expected to be 500, compared with the present 300. The university's action climaxed a concerted two-year effort by a group of lawmakers and health officials to head off a growing shortage of doctors in Michigan. That expansion of Wayne's College of Medicine could be done practically and economically was substantiated by a report to a legislative study committee on higher education by William T. Sanger, Sc.D., chancellor of the Medical College of Virginia, Richmond. The report said that Wayne's medical school should be expanded to accommodate 200 entering students a year before consideration is given to a third medical school in Michigan.

NEW YORK

Permits for Farm Labor Camps.—Owners of more than 1,060 farm labor camps in New York State reportedly are affected by an amendment of the Public Health Law which requires that permits be obtained to operate such camps. Dr. Herman E. Hilleboe, State Health Commissioner, announced that the State Legislature enacted the amendment and that the provisions for the permits are outlined in the State Sanitary Code, which sets up specific requirements concerning housing, fire hazards, bathing and toilet facilities, food handling and food storage facilities, water supply, and sewage disposal at farm labor camps. A new permit must be obtained each year before a farm labor camp is opened. Camps are inspected regularly to insure compliance with the Sanitary Code regulations. Information may be obtained from the State Health Department, 84 Holland Ave., Albany 8, N. Y.

New York City

Science Writing at Columbia.—Columbia University's advanced science writing program will start in September on an enlarged scale made possible by a 3-year $100,000 grant from the Rockefeller Foundation. The pilot financing was a 2-year, $70,000 grant from the Alfred P. Sloan Foundation. The combined financial support provides for 6 to 8 fellowships the first year and 10 or more in each of the two following years. The stipends will cover, in addition to tuition and fees, up to about $4,400 travel and living expenses for the academic year. In general the program will include participation in regular or specially arranged science courses or seminars under Columbia's faculties of pure science, medicine, or engineering; organized study of selected research and developments projects in the New York area; special meetings with both university and industrial research leaders; and special writing, some of it for publication. All participants will be expected to undertake a major research writing project in addition to regularly assigned writing.

Dedicate Mental Health Clinic.—Dr. Gunnar Gunderson of LaCrosse, Wis., President-Elect of the American Medical Association, addressed a service of dedication for the Mental Health Clinic of the Lutheran Medical Center in Brooklyn recently. Opened last September, the clinic is directed by Dr. Paul A. Qualben, a psychiatrist, and John P.

Kildahl, Ph.D., a psychologist, both, also ordained pastors of the Evangelical Lutheran Church. The clinic is now providing about 45 hours per week of treatment to persons from all sections of the metropolitan New York area. It conducts a program of community education through lectures to local groups and seminars for clergy. Other participants in the dedicatory service were Dr. Thurman B. Givan, president, New York State Medical Society; F. Eppling Reinartz, president, National Council; and the Rev. C. O. Pedersen, president, Atlantic Circuit, Evangelical Lutheran Church. The Lutheran Medical Center includes a general hospital, maternity ward, nursing school, an intern program, and 14 other clinics.

PENNSYLVANIA

Philadelphia

Appoint Chairman of Anatomy Department.—Andrew J. Ramsay, Ph.D., has been appointed professor and head of the department of anatomy and director of the Daniel Baugh Institute of Anatomy of Jefferson Medical College. Dr. Ramsay served as an assistant and instructor in histology and embryology at Cornell University, New York City, from 1930 to 1936. He became assistant professor of embryology at Jefferson Medical College in 1937, associate professor in 1941, and professor in 1948.

Grant for Cancer Research.—The Fels Research Institute of the Temple University School of Medicine has been awarded a grant of $195,488 for its next fiscal year beginning July 1 by the Fels Fund. The institute, established by the late Samuel S. Fels, of Philadelphia, is dedicated to research in gastroenterology and cancer. An additional grant of $29,000 has been awarded the institute by the Fels Fund toward the cost of a new laboratory, now nearing completion. The institute is under the direction of Dr. Harry Shay, professor of clinical medicine at Temple University.

Medical Arrangements for Orchestral Tour.—To insure the health of Philadelphia Orchestra members during the eight-weeks' tour to 14 countries overseas, the orchestra has taken along its personal physician, Dr. Milton J. Freiwald, ophthalmologist on the faculty of Jefferson Medical College. The president of Merck, Sharp and Dohme presented a medical case to Conductor Eugene Ormandy and Dr. Freiwald prior to the orchestra's departure May 10. The case contained drugs for emergencies and a surgical kit. With aid of the city's health department, orchestra personnel were inoculated for smallpox, typhus, and typhoid. Dr. Freiwald has had the assistance in these arrangements of Dr. George F. Lull, secretary of the American Medical Association; Dr. Paul Van de Calseyde, director of the World Health Organization in the United Nations regional office, Copenhagen; and Dr. Louis H. Bauer, secretary general, World Medical Association, New York City.

GENERAL

Prevalence of Poliomyelitis.—According to the National Office of Vital Statistics, the following number of reported cases of poliomyelitis occurred in the United States, its territories and possessions in the weeks ended as indicated:

Area	May 31, 1958 Paralytic Type	May 31, 1958 Total Cases	June 1, 1957 Total
New England States			
Maine	..	..	..
New Hampshire	..	..	..
Vermont	..	..	..
Massachusetts	..	..	..
Rhode Island	..	..	..
Connecticut	1	1	..
Middle Atlantic States			
New York	..	1	1
New Jersey	..	..	..
Pennsylvania	..	..	..
East North Central States			
Ohio	..	..	1
Indiana	..	..	..
Illinois	1	4	..
Michigan	..	..	3
Wisconsin	..	..	..
West North Central States			
Minnesota	..	..	..
Iowa	..	1	..
Missouri	..	..	1
North Dakota	..	..	..
South Dakota	..	..	..
Nebraska	..	..	..
Kansas	..	..	1
South Atlantic States			
Delaware	..	..	..
Maryland	..	..	..
District of Columbia	..	..	..
Virginia	1	1	2
West Virginia	..	..	..
North Carolina	..	1	..
South Carolina	..	..	2
Georgia	..	..	..
Florida	3	7	..
East South Central States			
Kentucky	..	..	1
Tennessee	1	1	..
Alabama	..	..	..
Mississippi	..	1	3
West South Central States			
Arkansas	..	..	2
Louisiana	..	..	4
Oklahoma	2	5	1
Texas	4	11	32
Mountain States			
Montana	..	..	..
Idaho	..	..	..
Wyoming	..	..	..
Colorado	..	..	1
New Mexico	..	..	..
Arizona	..	1	2
Utah	..	..	..
Nevada	..	..	..
Pacific States			
Washington	..	..	..
Oregon	..	..	1
California	4	6	6
Territories and Possessions			
Alaska	..	..	..
Hawaii	4	4	..
Puerto Rico	1	1	..
Total	22	46	64

Six-Member Society Strong on Civic Duty.—The Bosque County Medical Society (Texas) has a membership of six doctors and they are holding—or have held—27 positions in local government, business, and civic life. Among the six are a past-president of the Texas Board of Education, a former mayor, two school board trustees, two city council members, two bank directors, a director of Texas Good Roads Association, and a finance company director. Altogether, they put in over 140 hours a month in civic activities.

Awards to Rehabilitation Workers.—Fellowship and scholarship awards for the specialized training of 34 professional workers who are giving rehabilitation services to the crippled have been announced by the National Society for Crippled Children and Adults and two national women's fraternities, Alpha Chi Omega and Alpha Gamma Delta. Alpha Chi Omega financed 14 scholarship awards to doctors, therapists, teachers, administrators, and other specialists to take advanced specialized training for work with the cerebral palsied at five medical schools, hospitals, and universities this summer. Alpha Gamma Delta provided funds for 20 fellowships to counselors, guidance teachers, employment interviewers, placement personnel, and other professional workers who will receive specialized training in counseling and placement of severely handicapped persons including those with cerebral palsy in a special four-week training course at the Institute of Physical Medicine and Rehabilitation, New York University–Bellevue Medical Center, June 16-July 11.

Institute for Muscle Disease in New York City.—Construction started recently on a $3,700,000 Institute for Muscle Disease following ground-breaking ceremonies attended by civic officials and officers and members of Muscular Dystrophy Associations of America, Inc., which is sponsoring the institute. The structure is located on 71st Street between York Avenue and East River Drive in Manhattan. The institute will conduct research and correlate medical data from other sources toward finding a cause and cure for muscular dystrophy and related diseases. MDAA officials participating in the ceremony included president William Mazer and Dr. Ade T. Milhorat, chairman of the MDAA medical advisory board. The institute was made possible through public contributions to the November "March for Muscular Dystrophy." The general laboratories, occupying 5 of the 11 floors, are so arranged that alterations to meet future needs can be made with a minimum of expense. The building will be air-conditioned throughout. A program of research presently maintained by MDAA includes nearly 100 research projects in this country and abroad. The association also provides clinical care and patient services through its chapters.

Society News.—The **American Urological Association** has elected the following officers: president, Dr. Adolph A. Kutzmann, Los Angeles; president-elect, Dr. William M. Coppridge, Durham, N. C.; secretary, Dr. Samuel L. Raines, Memphis, Tenn.; treasurer, Dr. Grayson L. Carroll, St. Louis; and historian, Dr. Wirt B. Dakin, Los Angeles. The 1959 meeting will be held in Atlantic City, N. J., April 20-23, with headquarters at Chalfonte–Haddon Hall.—The **Southern Neurosurgical Society** has made the following officer changes: Dr. James G. Arnold Jr., of Baltimore, succeeded Dr. William F. Meacham, of Nashville, as president; Dr. Charles L. Neill, of Jackson, was elected vice-president; the secretary-treasurer, Dr. C. Douglas Hawkes, of Memphis, has one more year of a three-year term to serve. The 11th annual meeting of the society will be held at the Americana, Bal Harbor, Miami Beach, Fla., Jan. 23-24, 1959.—The **Mid-Central States Orthopaedic Society** has elected the following officers for 1958-1959: president, Dr. Werner P. Jensen, Omaha; vice-president, Dr. Harry O. Anderson, Wichita; past-president, Dr. Francis W. Carruthers, Little Rock; and secretary-treasurer, Dr. Henry O. Marsh, Wichita. The next meeting of the society will be held in Omaha about the first week in April, 1959.

Awards for Nutrition Essays.—Dr. Edgar F. Dunton and Dr. James R. Smith, of the University of Texas Medical Branch, Galveston, won the grand prize of $750 in the J. B. Roerig and Company's nationwide nutrition essay contest for medical students, interns, and resident physicians with their essay, "High Protein Feeding in the Severely Burned Patient." Three other prize winners each received $250; Jack William Hall, a junior student at Medical College of Virginia, Richmond, for "Nutritional Aspects of the Anemic State"; Vincent J. Fisher, a senior at New York State University College of Medicine, Brooklyn, for "Kwashiorkor, A Challenge in Preventive Medicine"; and Dr. J. Sidney Fulmer, an intern at Greenville General Hospital, Greenville, S. C., who won in the intern category for a paper on obesity, "The Pickwickian Syndrome—A Nutritional Disease." Contest judges were Dr. Robert S. Goodhart, scientific director, National Vita-

min Foundation, New York; Dr. Robert E. Olson, head, department of biochemistry and nutrition, Graduate School of Public Health, University of Pittsburgh; and Max K. Horwitt, Ph.D., director of biochemical research, Elgin State Hospital, Elgin, Ill. J. B. Roerig and Company is a pharmaceutical division of Charles Pfizer and Company, Inc., New York City.

EXAMINATIONS AND LICENSURE

MEDICAL SPECIALTY BOARDS

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral Examination.* San Francisco, Sept. 29-Oct. 3, and Phoenix, April 5-10, 1959. The 1959 written examination will be given in various locations in the United States and Canada, July 17. The final date for filing application for the 1959 written examination is six months prior to the examination. There is no filing deadline for oral examinations. Sec., Dr. Curtiss B. Hickcox, 217 Farmington Ave., Hartford 8, Conn.

AMERICAN BOARD OF DERMATOLOGY: *Written. Several Cities,* June 30. *Oral.* Detroit, Oct. 17-19. Final date for filing all applications is April 1. Sec., Dr. Beatrice Maher Kesten, One Haven Ave., New York 32.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written.* Oct. 20, 1958. *Oral.* Philadelphia, April 23-26; San Francisco, June 18-21; Chicago, Oct. 13-16. Sec.-Treas., Dr. William A. Werrell, One West Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY: Examination given twice annually, in the spring and fall. In order to be eligible a candidate must have his application filed at least six months before the examination time. Sec., Dr. Leonard T. Furlow, Washington University School of Medicine, St. Louis 10.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: Applications for certification, new and reopened, Part I, and requests for re-examination Part II, are now being accepted. All candidates are urged to make such application at the earliest possible date. Deadline date for receipt of application is September 1, 1958. No application can be accepted after that date. It should be noted by prospective candidates that the deadline date in 1959 is August 1. Sec., Dr. Robert L. Faulkner, 2105 Adelbert Road, Cleveland 6.

AMERICAN BOARD OF OPHTHALMOLOGY: *Written,* qualifying test (Part I), January 1959. Final date for filing application is July 1, 1958. *Oral Examinations 1958* (Part II): San Francisco, June 17-21; Chicago, Oct. 17-22. Sec., Dr. Merrill J. King, Box 236, Cape Cottage Branch, Portland, Maine.

AMERICAN BOARD OF ORTHOPAEDIC SURGERY: *Part II.* Chicago, Jan. 21-23, 1959. Deadline for receipt of applications is Aug. 15. Sec., Dr. Sam W. Banks, 116 South Michigan Avenue, Chicago 3.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* Chicago, Oct. 6-10. Final date for filing application was April 30. Sec., Dr. Dean M. Lierle, University Hospitals, Iowa City.

AMERICAN BOARD OF PATHOLOGY: Chicago, Oct. 30-Nov. 1. Final date for filing application is Sept. 30. Sec., Dr. Edward B. Smith, Indiana University Medical Center, 1100 W. Michigan St., Indianapolis 7.

AMERICAN BOARD OF PEDIATRICS: *Oral.* Chicago, Oct. 24-26 and New York, Dec. 5-7. Sec., Dr. John McK. Mitchell, 6 Cushman Road, Rosemont, Pa.

AMERICAN BOARD OF PLASTIC SURGERY: *Oral and Written.* Chicago, Oct. 9-11. Final date for receipt of case reports is July 1. Corresponding Secretary, Mrs. Estelle E. Hillerich, 4647 Pershing Ave., St. Louis 8.

AMERICAN BOARD OF PROCTOLOGY: *Oral and Written, Parts I and II.* September 1958. Final date for filing application is March 15. Sec., Dr. Stuart T. Ross, 520 Franklin Ave., Garden City, N. Y.

AMERICAN BOARD OF PSYCHIATRY AND NEUROLOGY: New York City, Dec. 15-16; New Orleans, Mar. 16-17. Training credit for full time psychiatric and/or neurologic assignment in unapproved military programs or services between the dates of Jan. 1, 1950 and Jan. 1, 1954 will be terminated on Jan. 1, 1959. Sec., Dr. David A. Boyd, 102-110 Second Ave. S. W., Rochester, Minn.

AMERICAN BOARD OF RADIOLOGY: *Regular Examination in Radiology.* Washington, D. C., Dec. 8-12. Final date for filing application is July 1. Sec., Dr. H. Dabney Kerr, Kahler Hotel Bldg., Rochester, Minn.

AMERICAN BOARD OF SURGERY: Written examinations (Part I) will be held at various centers in the United States, Canada, Hawaii, Puerto Rico, and certain military centers abroad on December 3. The date of the Fall examination in *Part I* has been changed from the last Wednesday of October as announced in its current Booklet of Information to December 3, 1958. Thereafter, examinations in Part I will be held once annually, on the first Wednesday of December. The closing date for filing applications will be August 1. *Part II.* Baltimore, March 10-11. Sec., Dr. John B. Flick, 1617 Pennsylvania Blvd., Philadelphia 3.

BOARD OF THORACIC SURGERY: The fall written examination will be given in September 1958 and closing date for registration is July 1. Registration for the fall oral examination closes July 1.

AMERICAN BOARD OF UROLOGY: *Written Examination.* Twenty-five cities throughout the country, Dec. 5. The oral will be given in Chicago in February 1959. Sec., Dr. William Niles, Wishard, Jr., 30 Westwood Road, Minneapolis 26.

DEATHS

Adamsons, Oscar Karlis Sr. ✙ Staten Island, N. Y.; Universität Bern Medizinische Fakultät, Switzerland, 1914; interned at St. Vincent's Hospital and served a residency at the Sea View Hospital in Staten Island; associated with the department of correction in New York City; died in New York City April 29, aged 69, of carcinoma of the stomach.

Allen, Charles Insley Sr. ✙ Wadesboro, N.C.; Columbia University College of Physicians and Surgeons, New York City, 1913; veteran of World War I; on the staff of the Anson County Hospital; president of the Bank of Wadesboro; died April 10, aged 67, of coronary occlusion.

Allen, Sylvia ✙ Kansas City, Mo.; Columbia University College of Physicians and Surgeons, New York City, 1926; on the faculty of the University of Kansas School of Medicine, Kansas City, Kan.; member of the American Psychoanalytic Association and the American Psychiatric Association; formerly associated with Menninger Clinic in Topeka, Kan.; died in the Research Hospital April 15, aged 66, of heart disease.

Barkan, Otto ✙ San Francisco; Ludwig-Maximilians-Universität Medizinische Fakultät, Munchen, Bavaria, Germany, 1914; specialist certified by the American Board of Ophthalmology; member of the American Academy of Ophthalmology and Otolaryngology and the Association for Research in Ophthalmology; served on the faculty of Stanford University School of Medicine; in 1954 the Section of Ophthalmology of the American Medical Association awarded him the Lucien Howe Medal for research in ophthalmology and allied branches; veteran of World War I; associated with St. Joseph's and Stanford University hospitals; died April 26, aged 71, of cerebral hemorrhage.

Bauer, Otto Michael ✙ Forest Hills, N. Y.; Medizinische Fakultät der Universität, Vienna, Austria, 1919; died March 27, aged 64, of acute coronary occlusion, coronary arteriosclerotic heart disease, cerebral arteriosclerosis, and cerebral thrombosis.

Benner, Charles Russell ✙ Chicago; Northwestern University Medical School, Chicago, 1905; on the staff of the Englewood Hospital, where he died April 29, aged 78, of carcinoma of the rectum with metastasis.

Blair, John Calvin, Kerens, Texas; University of Louisville (Ky.) Medical Department, 1892; died April 10, aged 90.

✙ Indicates Member of the American Medical Association.

Brennan, Thomas Francis, Lowell, Mass.; Kansas City (Mo.) University of Physicians and Surgeons, 1929; died in St. John's Hospital April 10, aged 53.

Bryan, William Wright ✙ Atlanta, Ga.; Emory University School of Medicine, Atlanta, 1932; clinical associate professor of radiology at his alma mater; specialist certified by the American Board of Radiology; member of the Radiological Society of North America and the American College of Radiology; vice-chairman, Section on Radiology, American Medical Association, 1957-1958; on the staffs of the Ponce de Leon Ear, Nose and Throat Infirmary and Grady Hospital; died April 10, aged 49, of a heart attack.

Carter, Donald Earl ✙ Washington, D.C.; Atlanta College of Physicians and Surgeons, 1913; service member of the American Medical Association; during World War I served as a captain in Great Britain's Royal Army Medical Corps, and was decorated by King George V with the Military Cross; associated with the Veterans Administration; died in the George Washington University Hospital April 14, aged 63.

Case, Clarence E. ✙ Ashtabula, Ohio; Western Reserve University Medical Department, Cleveland, 1895; fellow of the American College of Surgeons; medical examiner for the New York Central System for many years; associated with the Ashtabula General Hospital; a charter member and first president of the Ashtabula Rotary Club; died April 9, aged 87, of squamous-cell carcinoma of the hands.

Clough, William Plummer ✙ New London, N.H.; Dartmouth Medical School, Hanover, 1911; veteran of World War I; for many years town health officer; on the staff of the New London Hospital, where he died April 9, aged 78.

Condon, Stanley ✙ Detroit; Wayne University College of Medicine, Detroit, 1943; interned at Los Angeles County Hospital in Los Angeles; served a residency at Providence Hospital in Detroit; captain in the medical corps of the U. S. Air Force Reserve from June, 1953, to June, 1955; associated with St. John and Holy Cross hospitals; died April 5, aged 40, of a cardiovascular accident.

Dawkins, James Toliver, Birmingham, Ala.; University of Alabama School of Medicine, Mobile, 1909; served on the staffs of the Birmingham Baptist Hospital, West End Branch, and South Highlands Infirmary; died April 6, aged 76, of a heart attack.

DeLoatch, Mahlon Wingate, Tarboro, N. C.; Medical College of Virginia, Richmond, 1928; past-president of the Edgecombe–Nash Counties Medical Society; on the staff of the Edgecombe General Hospital, where he died April 12, aged 54, of coronary occlusion.

Doering, Valentine Theodore, Fort Madison, Iowa; St. Louis University School of Medicine, 1911; an associate member of the American Medical Association; served as city physician; on the staff of the Sacred Heart Hospital; died in St. Louis, April 1, aged 77, of pneumonia.

Drosin, Louis, New York City; Baltimore Medical College, 1905; member of the Medical Society of the State of New York; associated with the Beth David Hospital; died April 17, aged 76, of cerebral embolism.

Duff, John, La Jolla, Calif.; Tufts College Medical School, Boston, 1916; specialist certified by the American Board of Urology; member of the American Urological Association; fellow of the American College of Surgeons; served in the regular Navy; for many years practiced in New York City, where he was clinical professor of urology at the New York Medical College, Flower and Fifth Avenue Hospitals and professor of urology, New York Polyclinic Medical School and Hospital, and was associated with the Morrisania Hospital; died in the Mercy Hospital in San Diego, April 20, aged 64, of bronchogenic carcinoma.

Dwyer, Christopher Edward ✟ Waterbury, Conn.; Georgetown University School of Medicine, Washington, D. C., 1925; past-president of the Waterbury Medical Society and of the New Haven County Medical Society; served as president of the board of health; veteran of World War II; on the staff of Waterbury Hospital, where he died April 18, aged 59, of hypertensive heart disease.

Ehlman, Frank H., Milwaukee, Wis.; Milwaukee Medical College, 1899; died in Pewaukee April 16, aged 86, of arteriosclerotic heart disease.

Files, Ernest Woodbury, Portland, Maine; Medical School of Maine, Portland, 1905; fellow of the American College of Surgeons; for many years chief of the gynecological service at the Maine General Hospital; associated with the Webber Hospital in Biddleford and the Mercy Hospital; died April 10, aged 76.

Goodman, James Edwards Jr., Bradenton, Fla.; University of Pennsylvania Department of Medicine, Philadelphia, 1902; formerly practiced in Warrensburg, N.Y.; died Feb. 22, aged 86.

Grant, Iva Bouslough, Chicago; Kansas City (Mo.) Hahnemann Medical College, 1913; died in the Chicago Wesley Memorial Hospital April 17, aged 60, of acute myocardial infarction and arteriosclerotic heart disease.

Gunn, Milus Liddell ✟ Harlan, Ky.; University of Louisville School of Medicine, 1920; specialist certified by the American Board of Otolaryngology; member of the American Academy of Ophthalmology and Otolaryngology; fellow of the International College of Surgeons and the American College of Surgeons; consulting ophthalmologist of Louisville and Nashville Railroad Company; on the staffs of the Harlan Memorial and Harlan hospitals; died April 3, aged 61, of acute myocardial infarction and coronary occlusion.

Hare, Milton Metcalfe, Saratoga, Calif.; College of Medical Evangelists, Loma Linda and Los Angeles, 1925; died in San Jose April 6, aged 73.

Hauser, Charles David, Youngstown, Ohio; University of Buffalo School of Medicine, 1896; past-president of the Mahoning County Medical Society and president of the Sixth Councilor District Assembly in 1921; fellow of the American College of Surgeons; veteran of World War I; associated with St. Elizabeth Hospital, where he died April 7, aged 82.

Hodgdon, Ola Wilfred, Franklin, N.H.; Boston University School of Medicine, 1904; died in the Franklin Hospital April 5, aged 82, of arteriosclerotic heart disease and uremia.

Holleran, James Francis, Los Angeles; University of Southern California College of Medicine, Los Angeles, 1908; member of the American Academy of General Practice; served on the faculty of College of Medical Evangelists; associated with the Queen of Angels Hospital; died April 10, aged 72, of old myocardial infarctions and arteriosclerosis.

Hopkins, Percy Isaiah ✟ Dothan, Ala.; Vanderbilt University School of Medicine, Nashville, Tenn., 1899; fellow of the American College of Surgeons; associated with Moody and Frasier Ellis hospitals; died April 4, aged 78.

Houck, George E. ✟ Roseburg, Ore.; University of Oregon Medical School, Portland, 1890; past-president of the Southern Oregon Medical Society; fellow of the American College of Surgeons; formerly member of the city council, mayor and city and county health officer; served in France during World War I; at one time member and president of the state board of health; associated with the Mercy Hospital; died in Portland April 14, aged 92.

Howard, Emil W. ✦ Corvallis, Ore.; St. Louis College of Physicians and Surgeons, 1908; fellow of the American College of Surgeons; veteran of the Spanish–American War; associated with the Good Samaritan Hospital; died April 16, aged 80, of coronary thrombosis.

Kerwick, Joseph Maurice ✦ New Hampton, Iowa; State University of Iowa College of Medicine, Iowa City, 1920; died April 7, aged 66, of myocardial failure.

Kump, Albert Barker ✦ Bridgeton, N.J.; born in Bridgeton Sept. 9, 1908; University of Maryland School of Medicine and College of Physicians and Surgeons, Baltimore, 1938; member of the House of Delegates of the American Medical Association from 1953 to 1955; fellow of the International College of Surgeons; member of the Industrial Medical Association; president of the Medical Society of New Jersey, of which he was at one time second vice-president; past-president of the Cumberland County Medical Society; since 1940 medical director of the Bridgeton Plant of the Owens–Illinois Glass Company; chief of the department of obstetrics at Bridgeton Hospital since 1946 and was a member of the surgical staff; died April 18, aged 49, of bronchogenic carcinoma.

Landis, Charles Caldwell ✦ Chico, Calif.; George Washington University School of Medicine, Washington, D. C., 1912; vice-president and co-founder of the Feather River Sanitarium and Hospital in Paradise; associated with the Enloe Hospital; vice-president of the board of directors of the San Francisco Hospital; died in the Loma Linda Sanitarium and Hospital in Loma Linda March 10, aged 75, of heart disease.

Lubin, Solomon S., New York City; University and Bellevue Hospital Medical College, New York City, 1913; member of the American College of Chest Physicians and the American Trudeau Society; an associate member of the American Medical Association; associated with the Deborah Sanatorium in Browns Mills, N.J., Riverside, Mount Sinai, and Gouveneur hospitals; died in the Edgewater Hospital in Chicago April 15, aged 76, of arteriosclerotic heart disease.

Lucas, Isaac Marion ✦ Albany, Ga.; University of Louisville (Ky.) Medical Department, 1908; associated with the Phoebe Putney Memorial Hospital, where he died April 3, aged 76, of acute myocardial infarction.

Lyons, John James, Brooklyn; Long Island College Hospital, Brooklyn, 1898; veteran of World War I; died in the Veterans Administration Hospital March 20, aged 81, of pneumonia.

McCrary, John Henry, McAlester, Okla.; (licensed by years of practice); died March 6, aged 88, of coronary thrombosis.

Mercer, Clarence Mavel ✦ Battle Creek, Mich.; Jefferson Medical College of Philadelphia, 1907; fellow of the American College of Surgeons; on the staffs of the Battle Creek Sanitarium, Community Hospital, and Leila Y. Post Montgomery Hospital, where he died April 11, aged 75.

Merrill, Clyde Harold, Altadena, Calif.; Medical School of Maine, Portland, 1912; an associate member of the American Medical Association; member of the Massachusetts Medical Society; veteran of World War I; died April 2, aged 68, of cerebral vascular accident.

Miller, Phabiat M., New York City; Baltimore Medical College, 1898; died March 9, aged 85, of bronchopneumonia and arteriosclerotic heart disease.

Miller, William Theodore, Indianapolis; Indiana University School of Medicine, Indianapolis, 1918; on the staffs of St. Vincent's and Methodist hospitals; died April 9, aged 65, of congestive heart failure and arteriosclerosis.

Moore, Thomas David ✦ Memphis, Tenn.; born in Hopkinsville, Ky., Aug. 27, 1894; Vanderbilt University School of Medicine, Nashville, 1916; professor of urological surgery at the University of Tennessee College of Medicine; fellow of the Southeastern Surgical Congress and the American College of Surgeons, of which he was a member of the board of governors; president of the Clinical Society of Genito-Urinary Surgeons; member of the American Association of Genito-Urinary Surgeons; past-president and secretary of the American Urological Association and honorary member of the South-Central Section; honorary member of the Puerto Rico Urological Association; charter diplomate of the American Board of Urology and in 1949 elected as a member of the board of trustees; past-president and secretary of the American Urological Research Foundation, which he founded; veteran of World War I; attending urologist and in 1949 president of the staff of Baptist Memorial Hospital; died in Whitehall, Ark., April 16, aged 63, of coronary thrombosis.

Morris, Carlyle ✦ Metuchen, N. J.; University of Pennsylvania School of Medicine, Philadelphia, 1922; specialist certified by the American Board of Internal Medicine; fellow of the American College of Physicians; veteran of World Wars I and II; past-president of the Middlesex County Medical Association; associated with the Veterans Adminis-

tration Hospital in Metuchen and the Muhlenberg Hospital in Plainfield; died April 10, aged 62, of cerebral hemorrhage.

Munk, Cleorie Erwin ✱ Kendallville, Ind.; Eclectic Medical College, Cincinnati, 1912; served as president of the Northeastern Indiana Academy of Medicine; died in the McCray Memorial Hospital April 4, aged 73.

Murphy, John Campbell ✱ Aurora, Ill.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1904; veteran of World War I; associated with St. Joseph and Copley hospitals, and St. Charles Hospital, where he died April 9, aged 82, of bronchopneumonia, arteriosclerotic heart disease, and bleeding peptic ulcer.

Mussey, Robert Daniel ✱ Rochester, Minn.; born in Glendale, Ohio, Jan. 10, 1884; Medical College of Ohio, Cincinnati, 1908; emeritus professor of obstetrics and gynecology at the University of Minnesota Graduate School; for many years a member of the staff of the Mayo Clinic, where he became a member of the board of governors in 1933 and in 1937 was named board chairman; during World War I served as a captain, and then major, in the medical corps of the U. S. Army; specialist certified by the American Board of Obstetrics and Gynecology and served as a director of that board; president of the Minnesota Society of Obstetrics and Gynecology in 1937, the American Association of Obstetricians and Gynecologists in 1948, and the Central Association of Obstetricians and Gynecologists in 1938; member of the American Gynecological Society, Minnesota Academy of Medicine, the Society of the Sigma Xi, Alpha Omega Alpha and the Alumni Association of the Mayo Foundation; in 1937 chairman of the Minnesota Committee on Maternal Welfare; served as director of the American Committee on Maternal Welfare; for many years on the staff of St. Mary's Hospital, where he died April 20, aged 74, of cardiovascular accident.

Nachlas, I. William ✱ Baltimore; Johns Hopkins University School of Medicine, Baltimore, 1918; associate professor of orthopedic surgery at his alma mater; specialist certified by the American Board of Orthopaedic Surgery; member of the American Orthopaedic Association and the American Academy of Orthopaedic Surgeons; veteran of World Wars I and II; served on the staffs of Sinai, Mount Pleasant, Provident, Union Memorial, Women's, and West Baltimore General hospitals, and the Children's Hospital School; member of the American board of associate editors of the *Journal of Bone and Joint Surgery;* died in Johns Hopkins Hospital April 20, aged 63.

Natter, Alexander L., Woodside, N. Y.; Long Island College Hospital, Brooklyn, 1923; died in the Kew Gardens (N. Y.) General Hospital March 13, aged 60, of acute posterior-wall infarction and arteriosclerotic heart disease.

Nemirow, Martin, Passaic, N. J.; Eclectic Medical College of the City of New York, 1911; died in the St. Mary's Hospital, Passaic, April 17, aged 77.

Paley, Samuel Morris, New York City; University and Bellevue Hospital Medical College, New York City, 1921; member of the Medical Society of the State of New York; specialist certified by the American Board of Physical Medicine and Rehabilitation; veteran of World Wars I and II; formerly associated with the U. S. Public Health Service; died in the Veterans Administration Hospital March 25, aged 59, of bronchopneumonia, cardiovascular accident, and arteriosclerosis.

Paul, James Richard ✱ North Hollywood, Calif.; University of Nebraska College of Medicine, Omaha, 1942; veteran of World War II; member of the American Psychiatric Association; resigned from the regular U.S. Army Oct. 29, 1946; died March 28, aged 42, of bronchopneumonia.

Pogue, Richard Ewart ✱ Carson City, Nevada; College of Medical Evangelists, Loma Linda and Los Angeles, 1933; served as superintendent of the Cottage Hospital in Watertown, Minn., and on the staffs of the Fairview and Swedish hospitals in Minneapolis; died Feb. 22, aged 52, of chronic rheumatic heart disease.

Powell, Annie Monica Dunn, Louisville, Ky.; University of Bombay, India, 1892; formerly a medical missionary; died in the Jewish Hospital March 19, aged 88.

Power, Younger Lovelace ✱ Ilion, N. Y.; Medical College of Virginia, Richmond, 1932; served as mayor of Ilion; on the staff of the Ilion Hospital; died March 4, aged 51, of coronary heart disease.

Rake, Geoffrey William, New York City; born in Fordingbridge, England, Oct. 18, 1904; L. R. C. P., London and M. R. C. S., England, 1927; after serving at Guy's Hospital in London, joined the teaching staff of Johns Hopkins Hospital in Baltimore; later became a member of the research staff of the Rockefeller Institute for Medical Research, and spent a year as research associate in the Connaught Laboratories, University of Toronto; joined Squibb in 1937 as head of the microbiology division of the Squibb Institute for Medical Research, in New Brunswick, N. J., of which he became director; became medical research consultant to the E. R. Squibb & Sons Division of Olin Mathieson Chemical Corporation,

and director of the Squibb medical division; in 1956 named scientific director of the International division of Olin Mathieson Chemical Corporation; recipient of the Gold Medal in Medicine of the University of London; one of the original members of the virus and rickettsial study section and the syphilis study section of the U. S. Public Health Service; member of the Society of American Bacteriologists, Society for Experimental Biology and Medicine, American Society of Epidemiologists, American Association of Immunologists, Harvey Society, New York Academy of Medicine, and the Royal Society of Medicine; fellow of the American College of Physicians; served as mayor of Millstone, N. J.; in 1953 joined the staff of the University of Pennsylvania schools of medicine and veterinary medicine in Philadelphia, where he served as a member of the Wistar Institute of Anatomy and Biology; known for his research in virus diseases and tuberculosis; joint author with Dr. Harvey Blank, "Viral and Rickettsial Diseases of the Skin, Eye and Mucous Membranes of Man"; a contributor to scientific textbooks; died in the Princeton (N. J.) Hospital April 20, aged 53.

Rosenstein, Isaac, New York City; University and Bellevue Hospital Medical College, New York City, 1908; died March 28, aged 72, of cerebral thrombosis and arteriosclerosis.

Rosenzweig, Joseph, Brooklyn; New York Homeopathic Medical College and Flower Hospital, New York City, 1933; member of the Medical Society of the State of New York; veteran of World War II; died March 20, aged 49, of coronary thrombosis and hypertension.

Seaman, Charles LeRoy ✙ Cherokee, Iowa; Creighton University School of Medicine, Omaha, 1935; veteran of World War II; formerly city health officer; district surgeon for the Illinois Central Railroad; died April 5, aged 50, of acute coronary occlusion.

Silsby, Frederick Ward, Atlanta, Ga.; Western Pennsylvania Medical College, Pittsburgh, 1905; an associate member of the American Medical Association; member of the Medical Society of the State of Pennsylvania and the American Academy of Dermatology and Syphilology; formerly practiced in Tarentum, where he was associated with the Allegheny Valley Hospital; died April 8, aged 85, of coronary thrombosis, chronic nephritis, and diabetes mellitus.

Slay, Iris Joe, Purvis, Miss.; Memphis (Tenn.) Hospital Medical College, 1913; veteran of World Wars I and II; died April 20, aged 70 of coronary thrombosis.

Smith, Chandler White ✙ Captain, U.S. Navy, retired, Washington, D.C.; born in Urbana, Ohio, March 11, 1883; Hahnemann Medical College and Hospital of Philadelphia, 1907; commissioned in the medical corps of the U.S. Navy in 1908 as an assistant surgeon with the rank of lieutenant (jg); served on continuous active duty with the Navy Medical Department until he was placed on the retired list of Naval Officers on June 30, 1936; attained the rank of commander in 1925; recalled to active duty in a retired status in October, 1939, and served until 1946, attaining the rank of captain in 1943; during his more than 35 years active Naval service, served with the Medical Department of the Navy throughout the United States and abroad, and in ships of the fleet; at the time of his release to inactive duty in 1946 was serving on duty at the National Naval Medical Center in Bethesda, Md.; died in the U.S. Naval Hospital in Bethesda April 9, aged 75.

Spain, Robert Thomas ✙ Conrad, Iowa; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; served on the staff of the Evangelical Deaconess Home and Hospital in Marshalltown; died April 1, aged 82, of heart disease.

Stanford, James Willingham ✙ Cartersville, Ga.; Medical College of Georgia, Augusta, 1928; president of the Bartow County Medical Society; died Feb. 24, aged 56, of uremia, pyelonephrosis, and nephrolithiasis.

Strange, Shelby Phipps ✙ San Francisco; Cooper Medical College, San Francisco, 1912; for many years associated with the Southern Pacific General Hospital; died April 6, aged 82.

Stratte, John Joseph Jr., Modesto, Calif.; Rush Medical College, Chicago, 1942; served on the staffs of the San Joaquin Hospital in Bakersfield, Bret Harte Sanatorium in Murphys, and the DeWitt State Hospital in Auburn; died April 12, aged 44, of injuries received in an automobile accident.

Taylor, Walter Oglethorpe, Boston; College of Physicians and Surgeons, Boston, 1909; died April 3, aged 81.

Thigpen, Charles Alston ✙ Montgomery, Ala.; born in Greenville, Ala., Dec. 19, 1865; Medical Department of Tulane University of Louisiana, New Orleans, 1888; specialist certified by the American Board of Ophthalmology and the American Board of Otolaryngology; past-president of the Medical Association of the State of Alabama; member of the American Academy of Ophthalmology and Otolaryngology, American Laryngological, Rhinological and Otological Society, and the Association for Research

in Ophthalmology; fellow of the American College of Surgeons; in 1916 member of the House of Delegates of the American Medical Association; veteran of World War I; served on the staff of St. Margaret's Hospital; died April 23, aged 92, of heart disease.

Tucker, Gabriel, Rosemont, Pa.; born in Wheeling, W. Va., Nov. 3, 1880; Jefferson Medical College of Philadelphia, 1905; emeritus professor of bronchoscopy, esophagology, and laryngology surgery at the University of Pennsylvania Graduate School of Medicine and served as professor of bronchoscopy and esophagology at the University of Pennsylvania School of Medicine in Philadelphia; specialist certified by the American Board of Otolaryngology; an associate member of the American Medical Association and at one time secretary and chairman of its Section on Laryngology, Otology and Rhinology; member of the American Association of Thoracic Surgery, American Academy of Ophthalmology and Otolaryngology and was elected to its honor society, American Laryngological Association, American Laryngological, Rhinological and Otological Society, and the American Broncho-Esophagological Association, of which he was past-president; fellow of the American College of Surgeons; served overseas during World War I; formerly on the staff of the Graduate Hospital of the University of Pennsylvania where he was in charge of the Chevalier Jackson Bronchoscopic Clinic; associated with Misericordia Hospital, Bryn Mawr (Pa.) Hospital, Fitzgerald–Mercy Hospital in Darby, Abington (Pa.) Memorial Hospital, Children's Hospital, Jeanes Hospital, and the Germantown Dispensary and Hospital; died April 17, aged 77, of cardiac disease.

Twitchell, Benjamin E. ✟ Belleville, Ill.; American Medical College, St. Louis, 1891; past-president of the St. Clair County Medical Society; served as president of the U.S. Board of Pension Examiners, county physician and coroner of St. Clair County; on the staff of St. Elizabeth's Hospital; died April 14, aged 91, of arteriosclerotic heart disease.

Wallace, Henry, New York City; Long Island College Hospital, Brooklyn, 1890; an associate member of the American Medical Association; fellow of the American College of Physicians; veteran of the Spanish–American War; formerly on the staff of the Mountainside Hospital in Montclair, N. J.; died April 24, aged 89.

Warta, Joseph J., Omaha; John A. Creighton Medical College, Omaha, 1902; associate professor of ophthalmology at his alma mater; associated with St. Joseph's Hospital; died April 14, aged 81, of acute myocardial infarction.

Wassell, Corydon McAlmont, Little Rock, Ark.; born in 1883; University of Arkansas School of Medicine, Little Rock, 1909; for many years a medical missionary in China; at one time health officer of Pulaski County; commissioned as a lieutenant commander in the medical corps of the U. S. Naval Reserve in 1940; assigned to caring for wounded officers and men of the cruisers Houston and Marblehead; commended by the late President Roosevelt in his radio address on April 28, 1942, for heroism in Java; awarded the navy cross for evacuating 12 badly wounded American servicemen under heavy Japanese gunfire in Java; refusing to leave the men to certain capture, he evacuated them on March 1, 1942, under heavy fire from both aircraft and ground troops; retired as a rear admiral; his heroism during World War II was the theme of a novel and motion picture; died May 12, aged 74.

Watkins, J. Frank, Temple City, Calif.; University of Tennessee College of Medicine, Memphis, 1919; served on the staffs of the Behrens Memorial Hospital in Glendale and the French Hospital in Los Angeles; died in Covina March 22, aged 69, of a heart attack.

Whigham, Arthur Lee, Newville, Ala.; University of Alabama School of Medicine, Mobile, 1910; died April 4, aged 70, of rupture of abdominal aneurysm.

Williams, Angus S. ✟ Renton, Wash.; Medico-Chirurgical College of Philadelphia, 1899; member of the American Academy of General Practice; died in the Virginia Mason Hospital April 16, aged 87, of bronchopneumonia.

Williams, Gordon Darnall ✟ Weatherford, Okla.; University of Oklahoma School of Medicine, Oklahoma City, 1927; veteran of World War II; died April 1, aged 57.

Winn, William M. Jr. ✟ Clarksville, Va.; Medical College of Virginia, Richmond, 1911; died in Atlantic City, N.J., April 20, aged 69, of acute myocardial infarction.

Worth, Charles Mansfield ✟ Denver; Denver College of Physicians and Surgeons, 1907; died April 15, aged 89, of carcinoma of the throat with metastasis and arteriosclerosis.

Wotherspoon, Gordon ✟ Seattle; University of Glasgow Medical Faculty, Scotland, 1934; veteran of World War II; died April 19, aged 53.

Young, Edward Bradley, Zachary, La.; Medical Department of Tulane University of Louisiana, New Orleans, 1896; an associate member of the American Medical Association; died March 11, aged 86, of cardiac failure and cerebral accident.

FOREIGN LETTERS

AUSTRIA

Air Gun Injuries.—At the meeting of the Society of Physicians in Vienna on May 2, Dr. A. Gund reported on suicides committed with the aid of an air gun designed to render animals unconscious before slaughtering. The gun is placed directly against the head. In penetrating the cranium a bone chip of the caliber of the cartridge is punched out by the nose of the cartridge. The bone chip acting as secondary projectile is driven into the brain. The injury is fatal if the bone chip reaches the area of the third ventricle. Of two patients reported on one survived after an intracranial operation because the bone chip passed along the anterior base of the skull toward the posterior nares.

Inoculation Metastasis.—At the same meeting Dr. J. Glaninger said that the production of inoculation metastasis depends on the viability of the transmitted cells and the nature or susceptibility of the new bed. These factors are present when, for the purpose of resection of a carcinoma of the larynx, anesthesia is induced by peroral intubation. The consistency of the tracheal catheter and the slight pressure used with intubation are such that viable cells may be separated from the cancer and displaced into the lung. This applies especially if the tube must be forced past a stenotic area; otherwise the dissemination is hematogenous or lymphogenous.

Human Milk Center.—At the meeting of the Society of Pediatrics in April Dr. H. O. Juergenssen said that human milk represents the optimal food for the nursing infant and is an absolute necessity in feeding premature infants, dystrophic infants, and those with severe nutritional disturbances. The human milk center collects the surplus of milk from hypergalactic women, since wet-nurses are a thing of the past. Nurses, who have at their disposal small buses provided with cooling apparatus, collect the milk from the donors (about 2,000 per year) and from maternity wards daily. On the average nearly 1,000 liters are collected per month. As soon as the milk arrives at the center, it is examined for possible adulteration, acidity, and impurities. It is boiled for five minutes and then refrigerated. It is distributed only on prescription. The price is about $1.40 per liter. Because the supply sometimes exceeds the demand, various methods of preservation have been tried. Lyophilization is the only method which preserves the raw character of the milk and such thermolabile constituents as enzymes, inhibins, and vitamins. Once lyophilized, the milk can be stored at room temperature indefinitely, and requires little storage space.

Pulmonary Arteriovenous Aneurysm.—At the meeting of the Society of Physicians in Vienna on May 9, Dr. Wenzl stated that pulmonary arteriovenous aneurysm is an embryonal malformation in the pulmonary circulation, resulting in a right-to-left shunt. An operation is necessary because of the high mortality resulting from rupture of the aneurysm and cerebral complications. In the course of the operation the arterial oxygen saturation may be tested to determine the success of the operation. If reduction of the flow through the arterial branches that lead to the aneurysm results in normalization of the decreased arterial oxygen saturation, proof is provided that the shortcut circulation is completely interrupted. Extracardiac as well as cardiac causes may be responsible for the genesis of congenital cyanosis.

Dr. F. Schmidt said that an important factor in the production of central cyanosis and symptomatic polycythemia is the decreased oxygen content of the arterial blood. Hypoxemia frequently occurs in pulmonary diseases. The mechanisms leading to that occurrence can be determined by a combined examination of pulmonary function. The examination is performed with the aid of a spirometric ventilation test and an analysis of the arterial blood. The analysis of the arterial blood is performed during rest, after oxygen inhalation for at least 10 minutes, and during exercises with the ergometer bicycle. An insignificant influence on the arterial hypoxemia during oxygen inhalation is considered proof of a left-to-right shunt of at least 15% of the minute-time volume of the heart. Cyanosis is not manifested when anemia is present at the same time. Other mechanisms that lead to arterial hypoxemia, polycythemia, and cyanosis include the chronically deficient oxygen supply of the lung associated with chronic, spastic bronchitis and the "disturbance of diffusion" (alveolocapillary block) shown in patients with diffuse pulmonary fibrosis. Dr. H. Ellegast stated that roentgenography is an important factor in the diagnosis of pulmonary arteriovenous aneurysm. Single aneurysms present a particular roentgenographic and diagnostic problem. A more or less pronounced change in size of this vascular tumor is revealed by the Valsalva and

The items in these letters are contributed by regular correspondents in the various foreign countries.

Mueller tests. Pulsations can be defined by means of a kymogram. With the use of tomography, which should be carried out on two planes, it is usually possible to show the relationship of a shadow, which at first may have an atypical appearance with dilated afferent and efferent vessels.

Tuberculosis and Pregnancy.—At the same meeting Dr. Jentgens stated that statistics show that (1) pregnancy does not interefere with the treatment of tuberculosis, (2) the success of the treatment of tuberculosis during pregnancy depends on the understanding and full cooperation of the patient, and (3) the early detection of all persons with tuberculosis is important to the success of treatment. The family physician should advise his pregnant patients as to signs of tuberculosis. Fifty-one patients with extrapulmonary tuberculosis, including some with recent tuberculous spondylitis which required operation, were treated during pregnancy. In one patient nephrectomy had to be performed during pregnancy. All methods of treatment are applicable to pregnant patients with pulmonary tuberculosis. The same applies to chemotherapy and treatment by resection. No difference is made between the treatment of pregnant and nonpregnant patients. In a series of 21 pulmonary resections performed during pregnancy, all operations led to obliteration of the cavities and conversion of the sputum to negative. Birth and confinement were without complications in those patients. With modern method of treatment interruption of pregnancy because of tuberculosis is no longer indicated. After delivery the treatment for tuberculosis may have to be continued for several months. Operation if required should not be performed until two to three months after delivery.

958
167

CANADA

Talar Fusions.—Mustard and Laurin (*Canad. J. Surg.* 1:201, 1958) reviewed a series of 301 patients with fusions about the ankle and foot in children. They had good results in 73 to 90%, depending on the operation used. They found that the extra-articular subtalar fusion described by Grice was easily and safely obtained in patients 5 years of age. It was performed to maintain subtalar alignment and stability after correction of a valgus or varus deformity. It could be performed earlier if it was desired to discard a brace. After 8 years of age, it was best to defer fusion until a triple arthrodesis could be performed in patients at the age of 12. In the latter operation, internal fixation with staples was found useful and correction of muscle imbalance essential. A Lambrinudi fusion was found to provide good correction of idiopathic talipes cavus without sacrifice of length, but it should not be done for a paralytic talipes cavus. It provided good correction of dynamic and fixed talipes equinus after poliomyelitis or cerebral palsy. Ankle fusions alone were rarely indicated for paralysis in children. If necessary they can be performed by the Gallie technique without disturbing growth. For children with flail legs below the knees, patellar arthrodeses gave excellent results but were inadequate if the hips were unstable.

Radiation Hazards.—Johns and Wilson, (*Canad. M. A. J.* 78:571, 1958) investigated the gonadal dose of radiation received by persons in the mass chest roentgenography program in Ontario. They used paraffin wax phantoms with an ion chamber centered at a point representing the average position of the ovaries. A number of experiments indicated that the female gonadal dose received depended almost entirely on the distance from the iliac crest to the lower edge of the x-ray beam. It is therefore essential to know the exact location of the lower edge of the beam on each unit used. This was determined by the use of films and lead strips. In all units tested, the beam was found to extend below the screen. The investigators concluded that the gonadal dose may be reduced by (1) replacing all circular cones with rectangular cones and inserts; (2) ensuring that the beam does not extend below the screen; (3) placing the subject with the iliac crest as far below the screen edge as possible; and (4) increasing the speed of the camera screen and film and avoiding overexposure and underdevelopment. Use of a filter had little effect on the gonadal dose. These precautions have now been applied to all miniature film units in Ontario, and it has become evident that with them the gonadal dose from mass roentgenography of the chest may be reduced to 0.26 mr or 0.25% of the background irradiation, where it is probably not a significant hazard. Use of faster films when they become available will probably reduce the dose by a further factor of 2.

Myocardial Revascularization.—For several years, Vineberg and co-workers have treated coronary artery insufficiency by implantation of the internal mammary artery into the myocardium. They have had excellent results from this, but the method has its limitations, and they have therefore constantly searched for other methods of myocardial revascularization. Recently they reported on the use of Ivalon sponge application to the bared myocardium in animals in whom coronary insufficiency was induced by application of ameroid constrictors around the coronary vessels. Most control animals died within 27 days of myocardial ischemia, but all of 14 animals to whose myocardium the sheets of Ivalon sponge were applied lived well beyond the control series period, 11 of 14 being sacrificed two and a half to four months after operation. This time, in spite of the constriction of the coronary

arteries, there was no sign of myocardial infarction. Evidence was found of a connection between pericardial vessels, vessels in the interstices of the sponge, and myocardial sinusoids with direct connections leading into the lumen of the left ventricle. This operation was performed in one patient who was totally disabled, and, with use of 250 glyceryl trinitrate tablets a week, excellent results were obtained seven weeks after the operation.

Background and Problems of Medical Students.—Last year, Dr. J. S. Thompson, the executive secretary of the Faculty of Medicine of the University of Alberta, made a study of the economic and social backgrounds of 700 medical students. He has now investigated the circumstances of a smaller group in greater detail, mainly by the anonymous questionnaire method. He asked the students which quarter of the class they stood in and found that practically no one admitted to standing in the bottom quarter, so that the class divided itself into thirds. Dr. Thompson's sample consisted entirely of Alberta students, 61% of whom came from homes where the annual income was at or below the Alberta average of $5,082. Performance through medical school was closely correlated with the average marks on admission. Thus, those with an average mark on admission of over 70% rarely had to repeat a year, whereas of those with average admission marks of under 65% about 21% had to withdraw, another 21% had to repeat a year, and 12% had to write a supplementary examination.

Students were asked about their motivation in entering medicine. By and large, the reasons given fell into three categories: (1) 55% entered, at least partly, for the interest provided by the subjects and interest in life as a physician; (2) 42% noted some form of service to their fellows as a factor in their decision, five wishing to be medical missionaries; and (3) 39% admitted that social prestige and economic security entered into their decisions. Dr. Thompson also investigated the reasons of other students for not studying medicine, although they had thought about it. The commonest reasons were the student's poor academic record (130), insufficient funds (123), the length of the course (86), or a feeling that the rewards were not worth the money and effort (51). About 21% of medical students reported that financial problems might interfere with the completion of their course. The biggest sources of income were summer work and assistance from parents or wife. Only 23 of 202 students were putting themselves through medical school unassisted by other sources except minor scholarships. Only 25% of those who worked during the term believed that this work seriously interfered with their academic standing; 66% estimated that they would be in debt by the time they graduated. In the third and fourth years almost 50% of the students were married, and 37% of the married students had children. The added responsibilities of marriage did not appear to interfere with class standings. Over 50% of the entire sample reported no serious worries, 21% had financial worries, 13% had personal problems, and 9% worried about their health (7% worried about their mental stability).

Public Relations Workshop.—The Canadian Medical Association held its first public relations workshop in April. Participants included the Central Nucleus Committee for Public Relations and representatives of divisional public relations committees. There was also a session at which these physicians met with members of the press, radio, and television to discuss mutual problems. The concept of medical public relations is still in an early stage of development in most of Canada. Participants in the workshop discussed problems in relation to various groups of society, beginning with the politicians in federal and provincial legislatures. An additional effort will be made to acquaint these people with the viewpoint of organized medicine and to arrange for their continuous information by the provincial and national medical associations. Labor will also be provided with information on medical care. British Columbia is starting a survey to determine the public attitude to the medical profession in general. Nova Scotia has been concerned with the efforts of the chiropractors to obtain official recognition. The medical profession has taken steps to acquaint members of the press and the legislature with the exact nature of chiropractic and its reasons for opposing such recognition. Some divisions have arranged mediation committees or emergency call services, and others have prepared lists of spokesmen for contact with the press, radio, and television.

Wringer Injuries.—Lindsay and co-workers (*Canad. J. Surg.* 1:189, 1958) analyzed a series of 419 cases of wringer injury in children. In such an injury, a hand is caught between the rollers of a washing machine, resulting in contusion affecting all layers, friction producing superficial abrasion, and avulsion or shearing which separates the skin from the underlying fascia. A secondary force, namely the expanding hematoma, forms insidiously and may cause strangulation of the avulsed skin or pressure damage to nerves and muscles. The injuries may be classified as (1) cutaneous, (2) complex, with edema of all tissue layers, or (3) critical, with extensive skin loss and death of underlying tissue. In 80% of the present series the injury was mainly cutaneous and the victims could be treated as outpatients. All were reexamined in 12 to 24 hours to detect the development of progressive swelling or subcutaneous or subfascial hematoma. First-aid treatment consisted of putting the arm at rest in a sling and applying a loose, clean dressing. In mild cases the injured part was thoroughly cleansed, an

antiseptic applied, and a bland sterile petrolatum gauze dressing applied. Pressure dressing and elevation of the injured limb were recommended. In complex or critical cases, the patient was admitted to hospital, the skin lesions were treated first, and when the devitalized tissue became demarcated it was excised and the area covered with skin grafts. Hematomas were drained. Antibiotics and ACTH were of no benefit, and roentgenography was seldom necessary.

CHILE

Malignant Hypertension.—At the meeting of the Medical Society of Santiago in May Dr. Ricardo Cruz-Coke reported on a series of 284 unselected, hospitalized, hypertensive patients. The entire series was classified according to two scales of diastolic intensity: (1) a scale of diastolic blood pressures (DBP) devided into 6 levels of 15 mm. Hg each, ranging from 85 to 160 mm. Hg and over and (2) a scale of diastolic age and sex-adjusted scores (DAAS) divided into 6 degrees of 15 mm. Hg each, ranging from 0 to 75 mm. Hg and over. The two scales were correlated with the degree of retinal change, the frequency of electrocardiographic evidence of left ventricular hypertrophy and coronary artery disease, the frequency of congestive cardiac failure, and the frequency of the cerebral vascular accidents. The cause of the hypertension was not considered.

In the first scale 22% of the patients had a diastolic pressure over 130 mm. Hg (4th level); 26.5% of those with the retinal findings of malignant hypertension had a diastolic pressure under 130 mm. Hg; 83.3% of the patients with a diastolic pressure over 160 mm. Hg (6th level) had the retinal findings of malignant hypertension; and none of those with a diastolic pressure over 160 mm. Hg had normal eye grounds. Using the second scale 34.5% of the patients had a reading of over 45 mm. Hg (4th degree); only 10% of those with the retinal findings of malignant hypertension had a reading under 45 mm. Hg; only 46% of the patients with a reading over 75 mm. Hg (6th degree) had the retinal findings of malignant hypertension; and 16.6% of those with a reading over 75 mm. Hg had normal eye grounds.

Thus an incipient degree of malignant hypertension was revealed in those with a 4th degree DAAS reading. This degree is more significant than the corresponding level on the classic DBP scale in determining the beginning of malignant hypertension. The DAAS permits one to recognize patients with incipient malignant levels of DBP, before the disease produces retinal damage and left ventricular hypertrophy. It also shows the significance of high blood pressure in the aged. The frequency of congestive heart failure and left ventricular hypertrophy are related directly to the increase of the diastolic pressure, but the frequency of electrocardiographic evidence of coronary injury and of cerebral vascular accidents are not.

FRANCE

Psychosis in Epileptics.—G. Boudin and co-workers (*Semaine hôp. Paris* **35**:1231, 1958) studied 12 epileptics with acute psychosis. They were chosen on the basis of (1) presence of impairment of consciousness, delirium and hallucinations, and thymic perturbations, apart from mere confusion, (2) sudden onset, (3) rapid regression within about four days to three weeks, and (4) a history of epilepsy or observation of seizures. Electroencephalograms were made during psychotic episodes and periods of normal behavior on all patients. No specific structure of the psychic disorders was observed. Most patients were in a state of dream-like confusion with hallucinative or paranoid delirium. The most reliable finding was a history of epilepsy elicited from all the patients, but often with difficulty. In three patients the onset of the psychoses was closely related to an epileptic seizure. The electroencephalograms made in the course of the psychosis were compared with those recorded before and after the mental disorders. In one patient it was characteristic of a generalized centrencephalic epilepsy with bisynchronic peak-waves. The tracing was shown to be less active during the psychosis than before and after this period. In one patient it was a left-sided frontotemporal focus which disappeared during the psychosis. In the rest it was characteristic of an epilepsy involving the temporal lobes. In 8 of these the paroxysmal activity and the signs of suffering were aggravated during the psychosis. In four patients the daily electroencephalogram showed a permanent paroxysmal activity in the temporal region during the psychosis.

Hyperthyroidism.—R. Peycelon and co-workers (*Presse méd.* **66**:653, 1958) reported the results of 984 thyroidectomies. The follow-up study of 763 of these patients revealed 392 to be in good health and 288 with only a few minor neurovegetative disorders. Thus 80% of the patients in the follow-up were cured. Of the remaining 83 patients 17 had recurrences of hyperthyroidism and ocular sequelas, 8 had myxedema, 8 had paralysis of the recurrent laryngeal nerve, 8 had persistent hyperthyroidism, and 3 had tetany. Postoperative complication included hematoma with pressure on the trachea, injury to the recurrent laryngeal nerve, tetany, and thyroid crises, usually benign. The severe crises were treated with artificial hypothermia. Of the 984 patients 57 died, 27 in thyroid crisis; almost all of these deaths occurred before

1950. Operation is contraindicated in acute fulminating, hypertensive, and glycosuric forms of the disease. In those with the psychic forms or in whom ocular disturbances are predominant the treatment in each case must be decided on its merits. The three major indications for thyroidectomy are the forms with goiter, those refractory to medical treatment, and those accompanied by cardiac disturbances.

Mitral Stenosis.—J. Ducuing and co-workers (*Presse méd.* **66**:654, 1958) reviewed a series of 100 operations for mitral stenosis. In 40 patients the operation was performed by use of the finger alone; in 55 patients who had stenosis with thickening of the valve the operation was performed by using Dubost's dilator, and in 5 patients with funnel-like stenosis, in whom the valve had been completely destroyed, nothing could be done. In this series five patients died. One patient died during operation when the pulmonary artery was injured by the point of the auricular clamp, one after two operations because of injury to the left ventricle caused by the heel of the clamp, one after reoperation and tracheotomy because of pulmonary edema, and two because of thrombosis or embolism. Several accidents occurred during the operations. These included seven lacerations of the atrium, two ventricular fibrillations (both patients recovered), and one embolism of the posterior tibial artery. The results in 75% of the patients were considered excellent.

ICELAND

Iceland's Health.—The official health report for 1954, published in 1957, shows a record low death-rate, with only 1,064 deaths in a population of 156,033 (6.9 per 1,000) 39.8% of whom live in the capital. As causes of death, heart disease came first with 250 cases, followed by cancer with 198, and cerebral apoplexy with 156. There were 7 deaths among the 6,573 patients with measles and 2 among the 2,076 patients with pertussis. None of the 11 cases of poliomyelitis proved fatal. The 476 cases of gonorrhea marked a sharp rise in incidence, but there was no new case of syphilis. Diphtheria was conspicuous by its absence, and only one case of puerperal fever was reported in the past five years. In the capital, 82.5% of the confinements occurred in hospital, and more than 25% of the babies were born out of wedlock. There was no typhoid in 1954, but paratyphoid yielded a crop of 111 cases in addition to 41 carriers of Salmonella paratyphi B. This epidemic caused no deaths. The university performed 240 autopies, 64 for medico-legal reasons.

INDIA

Influenza in Children.—P. M. Udani (*Indian J. Child Health* **7**:4 [April] 1958) reported a series of 251 children with influenza observed in the pandemic in Bombay in May and June, 1957. The evidence that the illness in these children was due to an influenza virus was only circumstantial and epidemiological. It was hard to prove the diagnosis because of difficulties in isolating the virus and in carrying out serologic tests. The largest number of patients were seen in the first three weeks of the epidemic. No age was exempt, although the number of those under 3 months of age was relatively small. The youngest baby was 6 days old. He had fever and convulsions of one day's duration and died within a few hours of admission. Autopsy revealed typical lesions of influenza in the lungs. Another newborn baby had a temperature of 105 F (40.6 C) on the second day of life and died. His mother had influenza when he was born. There were 79 patients in the age group of 6 months to 3 years. In 156 of the children the disease was mild or moderately severe, and in 95 it was severe with complications; 12 of these had fulminating attacks and died in 3 or 4 days. Autopsy of these patients showed severe viral infection without secondary bacterial infection. The clinical findings were varied; 156 had an acute febrile attack with a sudden onset, and in 2 or 3 days in the moderately severe cases the findings resembled those of typhoid. Fifty-eight patients had the respiratory type of influenza. The upper respiratory tract was involved in most of them, but the lower respiratory tract was involved in all of these patients; 4 had tracheitis, 28 bronchitis, 21 bronchopneumonia and bronchiolitis, 2 bronchitis with pleuropneumonitis, 8 lobular pneumonia, 2 hemorrhagic pleurisy, and 10 predominantly interstitial pneumonia.

To what extent the lower respiratory lesions were due to the virus, or whether a superimposed bacterial infection caused these lesions, was difficult to say. In the 12 patients with fulminating attack there was no postmortem evidence of bacterial infection; pyogenic exudate was absent; and culture of the heart's blood was negative. In some who recovered, however, there was quick improvement with antibiotics, suggesting that bacterial infection played a secondary role. Fluoroscopy was performed on all patients and showed increased vascularity of the lungs and hilar regions in about 40%. Marked emphysema was seen in 50 patients; 8 had areas of pneumonitis; 2 had a small pleural effusion; 1 had pleurisy; and 1 had a patch of pleuropneumonia at the base of the lung. Nine had myocarditis with marked tachycardia, muffling of heart sounds, gallop rhythm, and an enlarged heart. One patient developed severe congestive cardiac failure and recovered within three weeks; five with

myocarditis died. In three of these autopsy revealed petechial hemorrhages in the pericardium and myocardium.

The condition of five patients with persistent vomiting was classified as gastric influenza; three of these later developed severe dehydration and encephalopathy, and two had diarrhea with dehydration. Both of the patients with diarrhea died in shock, and autopsy revealed typical pulmonary lesions—one had intestinal ulcerations. Five patients had hematemesis at the onset in association with other clinical features of the disease. One had a frank intestinal hemorrhage. One of these five died. Twelve patients had severe abdominal pain with gastrointestinal symptoms. One of these died and on autopsy showed marked enlargement of the mesenteric lymph nodes, with typical pulmonary lesions. A laparotomy was performed on another patient whose disease started as typical influenza. He later developed severe abdominal pain with signs of subacute intestinal obstruction; the mesenteric lymph nodes were acutely inflamed, and there were peritoneal adhesions. Twenty-four patients had findings suggestive of meningoencephalitis; 11 of these died. Polyneuritis was seen in one patient who was admitted in a semiconscious state with convulsions, pharyngeal congestion, and bronchitic, but no meningeal, signs. His calf muscles were tender on pressure and weak. The deep reflexes were diminished in all four limbs. Some patients with influenza in other members of the family had palatal weakness on one side with an influenzal onset. Lumbar puncture, performed on 23 patients, gave clear fluid under increased pressure. The spinal fluid proteins were increased in 7; sugar was slightly diminished in 2 and increased in 4; and 7 showed pleocytosis, predominantly lymphocytic. No organisms were isolated from the spinal fluid.

Three patients developed diabetes insipidus in the course of the disease; six had hyperpyrexia and all of these died; two had subnormal temperature and died in shock. Autopsy of these showed the findings of influenza. In nearly 200 patients the fever lasted 2 to 7 days; in 19 it lasted 8 to 14 days; and 21 had fever varying from two weeks to five months in duration. Hemorrhage occurred in 10 patients (severe epistaxis in 3, hematemesis in 5, severe internal bleeding in 1, and petechiae in 1). One had hemorrhagic mucus in the throat at autopsy. Some children developed a measle-like rash. Hepatitis and jaundice was seen in others. Postinfluenzal syndromes included frequent respiratory infections, malnutrition with recurrent respiratory infection and recurrent gastrointestinal upset, flare-up of an old tuberculous lesion, severe anemia, exhaustion, and mental retardation (especially in those with meningoencephalitis). The highest mortality occurred in the youngest infants. Although the patients were classified clinically in different groups according to the system involved predominantly, the children usually had multiple lesions. Thus children with meningoencephalitis also had severe pulmonary lesions. In spite of the varied clinical findings, severe hemorrhagic, interstitial bronchopneumonia was the most striking finding at autopsy.

ISRAEL

Vitamin B_{12} Determination.—Rachmilewitz and Stein (*Harefuah* **54**:169, 1958) stated that for the diagnosis of anemias and diseases of the liver, the determination of vitamin B_{12} in body fluids is of great value. Low serum vitamin B_{12} concentrations may be due to lack of intrinsic factor in the stomach, as in pernicious anemia and after gastrectomy. Disturbances in the absorption of vitamin B_{12} by the small intestine as in sprue, diverticulosis, or blind intestinal loops may also lead to vitamin B_{12} deficiency with low serum levels. Low vitamin B_{12} concentrations are also found in patients suffering from chronic malnutrition, low intake of vitamin B_{12}, and the anemia of pregnancy. A gradual decrease in serum vitamin B_{12} concentration precedes the development of anemia and the appearance of the characteristic morphologic changes in the bone marrow and peripheral blood. Megaloblastic anemia may be corrected by various means (folic acid or steroid hormones), but the vitamin B_{12} deficiency remains.

High serum vitamin B_{12} concentrations are found in viral and toxic hepatitis, the active stage of cirrhosis of the liver, chronic hepatic congestion due to heart failure, and malignant tumors invading the liver. Most of the serum vitamin B_{12} in patients with liver disease is bound to serum proteins, and the capacity of these proteins to bind vitamin B_{12} is increased. The increase of the vitamin B_{12} in the serum in liver disease is due to release of the stored vitamin from damaged liver cells. Since normal values of serum vitamin B_{12} are found in jaundice due to intrahepatic or extrahepatic obstruction, serum vitamin B_{12} determinations are helpful in differentiating hepatocellular from extrahepatic jaundice. In patients with liver disease and high serum vitamin B_{12} levels, the urinary excretion of the vitamin is increased. High serum vitamin B_{12} concentrations are found in myeloid leukemia but not in stem-cell leukemia or lymphocytic leukemia. All the vitamin B_{12} in the serum of patients with granulocytic leukemia is bound to protein. The urinary excretion of the vitamin in this disease is normal or below normal.

Rheumatic Fever Control.—Kagan and Brand (*Quart. Review "Harefuah"* **1**:10, 1958) reported that rheumatic fever annually afflicts 2,500 persons, mostly children, in Israel, and almost invariably damages the heart. The national incidence of the

disease is 1.5 per 1,000, but in Jerusalem it is 6 per 1,000. In 75% of the cases it strikes between the ages of 3 and 14. Since full recovery may be effected if the disease is recognized and treated early enough, a campaign of public education has been launched among physicians, teachers, and parents. The only exclusively rheumatic fever ward in the country is at the Bikur Holim Hospital in Jerusalem, with 30 beds. Such a ward is beneficial not only in providing a general program of study and therapy for victims but also in limiting the possibility of these children being infected with other diseases while in the hospital. Schools in Jerusalem may contribute to the incidence of rheumatic fever because they lack central heating.

Hospitalization at the Bikur Holim Hospital ranges from 6 to 13 weeks, with accommodation for convalescents available when needed at the WIZO Baby Home in Jerusalem. About 75 families in Jerusalem, with 100 rheumatic fever victims, have been "adopted" by members of the Rheumatic Fever Society. Food and warm clothing are distributed, jobs are found for an unemployed head of family, and healthier living quarters are arranged. The society also sends volunteer teachers to help children with lessons at home. Three "home to school" telephones have been installed in the homes of children with rheumatic fever, enabling them to participate in class lessons.

Poliomyelitis.—Dr. P. Yekutiel and co-workers reported that in the winter and spring of 1957 a large-scale immunization program against poliomyelitis was understaken in Israel. Salk vaccine, some of which was imported from the United States and some produced locally, was used. The program at first included infants and children 6 months to 3 years old. Of those eligible in this age group, 116,000 received two basic intracutaneous or subcutaneous inoculations of 0.3 to 0.5 ml. of vaccine, 5,500 received one inoculation, and 2,000 none. Later, infants 4 to 6 months old, children 3 to 4 years old, adults who immigrated from the English-speaking countries up to the age of 30, and children in this immigrant group were added to the program. A total of 22,000 of these received two basic inoculations, and several thousand received one inoculation. No vaccine was given between June 1, 1957, and Jan. 1, 1958, when booster inoculations were started. Clinical, epidemiological, and laboratory data were collected on each case of poliomyelitis that occurred in 1957. A total of 57 cases were reported. This number, compared to a five-year annual average of 650 cases in the years 1952 to 1956, constituted a reduction in poliomyelitis incidence of over 90%. Of the 57 cases 7 occurred in January before the effect of immunization could be expected; 22 occurred in nonimmunized infants less than 1 year old who were born in 1957 and, therefore, were not included in the program; 8 occurred in unvaccinated children over 4 years old; and 20 in the "campaign" age group. Of these 20 patients, 11 had received two inoculations of vaccine, 3 had received one inoculation, and 6 none. The immunization seems to have been very effective in reducing the incidence of poliomyelitis in the immunized infants and children. The high effectiveness of the immunization with Salk vaccine may have been due to the fact that almost 95% of the susceptible age groups had received two inoculations of vaccine prior to the poliomyelitis season.

JAPAN

Status of Tuberculosis.—Despite the use of PAS, streptomycin, isoniazid, and highly perfected chest surgery, morbidity from tuberculosis has not shown any sign of diminution, although the death rate has decreased. In other countries sanatoriums are being closed or undergoing a change of function for lack of tuberculosis patients. The causes for this situation will be found in the lack of public funds appropriated for tuberculosis control. Less than 30% of the patients with active cases are being treated in sanatoriums, and only slightly over 20% of all tuberculosis patients receive adequate treatment. Mass surveys are made only once a year, and only about 33% of the population are included in such surveys. As a consequence the number of active cases does not diminish. Each year an estimated 330,000 new cases develop. Tuberculosis hinders the nation's economic growth and is a potent cause of keeping the people impoverished, thus setting up a vicious circle.

Japanese B Encephalitis.—Each May and June there is an epidemic of Japanese B encephalitis. In the 1948 epidemic over 2,000 cases were reported, but in 1957 there were only 100. The disease reaches a peak every 10th year, so health authorities are prepared to vaccinate 500,000 children under 15 this year. The disease is especially dreaded because the case fatality rate is about 33% and the complications in those surviving include imbecility, epilepsy, and other permanent and completely disabling conditions. There is no permanent immunity, but among natives it is rarely seen after age 15.

Artificial Insemination.—The first successful insemination of a human subject was recorded nine years ago, but since then over 1,500 cases have been reported. No insemination of a single woman or a widow has been reported. A case in point recently came up. A young wealthy widow who lost her 7-year-old only child and did not wish to remarry requested a physician to arrange for artificial insemination. This was refused because any child born under such conditions would be judged to be illegitimate.

Isotopes and Tuberculosis.—Radioisotopes are being used as a tracer at Ochuja Sanatorium in Tokyo. Some of the questions to be studied are: 1. Will isotopes directly attack tubercle bacilli? 2. How does the pulmonary edema of tuberculosis occur? 3. How and by what route do streptomycin and other chemotherapeutic agents work? The results may revolutionize the treatment, according to Dr. Adachi.

Marriages Between Relatives.—Although marriages between relatives is prohibited by law, in certain districts where families have dwelt for many generations marriages between distantly related persons are common. It is generally believed that some of the hazards of such marriages include miscarriage, stillbirth, infant death, blindness, deafness, and hemophilia. While in other countries the percentage of such marriages is negligible, in Japan it is about 5%. To correct this situation more stringent laws are being drafted.

Medical Technicians to Be Licensed.—No modern hospital or clinic can operate without the services of the laboratory technician. To further improve their services the government has set a minimum standard of two years of college training as a prerequisite before the technical training can begin. Before being licensed a technician must now pass the state examinations.

NEW ZEALAND

Blood Studies of Maoris.—Lehmann and co-workers (*Nature, London* **181**:791, 1958) examined 92 Maoris, of whom 65 were not first-degree relatives. The aim was to obtain a gene pool which represented Maoris without white admixture. Eighty-five belonged to the Tuhoe and seven to the Arawa tribe. All were examined for the Diego blood group, for hemoglobins E and H, and for other abnormal hemoglobin types which can be detected by the sickling test or electrophoresis. In 84 samples a search was made for evidence of thalassemia by examining the cells morphologically, determining the alkali-resistant fraction of the hemoglobin and searching for an increased proportion of hemoglobin A_2. Recent investigations of Mongoloid populations showed in some of them a high incidence of hemoglobin E and of the Diego blood group. Hemoglobin E has been found in Siamese, Burmese, and northeastern Malaysians, and the highest frequencies of the Diego blood group have been found in North and South American Indians, Japanese, and Chinese. Hemoglobin H has been found in some Greeks, in a Jordanian Arab, notably in Chinese and Siamese, and occasionally in Philippinos and Malaysians. Thalassemia or Mediterranean anemia is not restricted to persons of Mediterranean origin, for a high incidence has been reported in Siamese and other Asiatic populations. Previous studies in the Australasian region had so far revealed no abnormal hemoglobins and no examples of the Diego blood group. In the present search no hemoglobin E, H, or any other abnormal hemoglobin, no Diego blood group, and no evidence of thalassemia were found in the Maoris. These findings distinguish the Maoris from the North and South American Indians and from the Siamese, Burmese, and Malaysians. It is of interest that the Diego factor was not found, in view of Heyerdahl's theory of the American origin of the Polynesians.

Identification of Narcotics.—Dr. O. H. Keys, government analyst for Otago and Southland, working in close cooperation with the University of Otago, devised a new technique for identifying narcotics which should be of great practical value. It is based on the bombardment of the material—as little as a fraction of a milligram—by a narrow beam of x-rays. A geiger counter records the angle of diffraction of the rays as a graph. Each material produces a distinctive graph, and it is a simple matter to compare the data with a specially devised reference file. The older chemical method of identification requires careful investigation, sometimes extending to two weeks. It has also the disadvantage that the substance isolated during the analysis is destroyed in the final identification. The new method has the advantages over the classical method that it is instantaneous, unequivocally accurate, and can classify a narcotic without destroying or consuming any of the material.

Lung Cancer.—According to a report from the statistical branch of the Health Department, not one factor but a combination of factors might be responsible for the increase of cancer of the lung and bronchus. The increase in the incidence of and mortality from cancer of the lung has been steady, with 286 pulmonary deaths from this cause in men in 1955 compared with 36 in 1936. The disease has been linked with cigarette smoking, atmospheric pollution, and certain occupational hazards. The incidence was greater in urban and highly industrialized areas than in rural areas, and immigrants from Great Britain showed a higher death rate from lung cancer than persons born in New Zealand of the same stock. The difference was greater in those who came here at a later age than in those who come to this country when young. The hypothesis is that immigrants are affected by their former environment. In contrast to the position in men, cancer of the lung in women is still uncommon in New Zealand. As it would be logical to expect the same relationship between lung cancer and smoking habits in women as in men, this is probably explained by the fact that there are few

women over 50 who have been heavy smokers for a long time. Most New Zealand women, in the ages at which lung cancer has the highest incidence among them, are nonsmokers and have always been nonsmokers. Few of even the heavy smokers have been smoking for long.

Infant Mortality in Cook Islands.—Dr. D. D. McCarthy of the University of Otago investigated the high infant death rate in the Cook Islands. In some of the islands the rate is 300 in every 1,000 live births. In New Zealand the rate is about 22 and among Maoris about 74. One startling finding, which may help other research workers and sociologists engaged in enhancing sanitation and welfare in the Southern Islands, was that the islands where the mortality is the highest are those in which the cash incomes are greatest. They have not yet learned what to do with their spare cash. Instead of spending their money on houses and giving more attention to their food, they spent it on clothes, wrist watches, and beer. Their extra spending money came mostly from pearl shells. The first preventive measure taken was to increase prenatal work and infant and child welfare. The Cook Islanders went through a bad economic period several years ago and developed a general sense of frustration. The change in their economic status was too rapid and they have not been able to adapt themselves to it.

SWEDEN

Professional Secrecy.—Since compulsory health insurance came into force on a national scale at the beginning of 1955, the medical profession has been confronted with problems of professional secrecy. The authorities concerned with the administration of health insurance wish to ensure its smooth working and to avoid abuses and to this end have indicated that on sending a patient to hospital his physician should give the reason for doing so. This means that he must more or less commit himself to a diagnosis which thus comes to the notice of the persons employed in the health insurance service. In *Svenska läkartidningen* for March 14, Dr. E. Svennilson pointed out how this proposal may embarrass the physician who sends a patient to hospital because he has become insane, has attempted to commit suicide, or is alcoholic, epileptic, or syphilitic. To protect his patients, the physician is tempted to make use of terminological inexactitudes, to use words comprehensible to scholars only, or to take refuge in the oracular "admission for observation." Svennilson sees no easy solution, but he insists that respect for professional secrecy is essential to the happy cooperation of physician with patient.

Courses in Public Health.—Physicians interested in public health and representing Denmark, Finland, Iceland, Norway, and Sweden meet every August in Gothenburg to discuss public health problems and to pool the experiences of their respective countries in this field. A further objective of these meetings, which enjoy financial support from WHO, is to train in public health physicians capable of holding important appointments in this specialty. Last fall the class of 22 was composed of 6 from Denmark, 4 from Finland, 1 from Iceland, 5 from Norway, and 6 from Sweden. One third had attended two earlier courses, another third one such course, and the rest were newcomers. For the first time the course was attended by two public health nurses. The range of subjects discussed on this occasion was wide and included the care of the aged, alcoholism, drug addiction, and suicides. The last week was spent in Oslo studying Norway's pioneer work on rehabilitation of the unfit, Norway's cancer register, and its welfare program for seamen. It is expected that from these courses a permanent school of public health will evolve.

Junior Physicians Meet.—The Swedish Association of Junior Physicians met in March in Upsala and reviewed the most salient features of the campaign to improve their lot. The chairman, Dr. Olof Johansson, drew attention to the agreement drawn up between the hospital authorities in June, 1957, and the holders of junior hospital appointments with reference to a pensions scheme. This agreement was provisional only. Another problem needing speedy solution concerned finding enough applicants for the many junior hospital appointments recently created. It was countered by an informal agreement between the parties most concerned to ration or rationalize these appointments. Another stumbling block has been the inadequate remuneration of the physicians who lecture to nurses. It was proposed that the fee of 25 Swedish crowns per hour be doubled. What is, perhaps, the most crying need of the medical profession is to be relieved of all the duties which can possibly be discharged by laymen.

Lidocaine for Epilepsy.—Dr. E. Bohm (*Nordisk medicin*, April 10, 1958) treated 48 epileptics with intravenous injections of a 1 or 2% solution of lidocaine. When this treatment was successful it took effect in 30 to 45 seconds—the time taken to complete the circulation of the blood. The injections did not disturb the patient's sense of consciousness, and when the attacks recurred, the treatment was repeated in the form of a continuous intravenous drip with saline or dextrose solution. A single dose of lidocaine was sufficient to arrest 11 of the 12 attacks of grand mal in 7 patients and 19 of the 29 Jacksonian attacks in 22 patients. Ten patients suffering from status epilepticus of the grand mal

type were given a continuous intravenous drip on 13 occasions in 7 of which the treatment was successful. Treatment was also successful on 14 of the 20 occasions on which it was given for status epilepticus of the Jacksonian type. The treatment was less effective in attacks of subcortical than in those of cortical origin.

Cycloserine for Tuberculosis.—Dr. I. Ståhle (*Svenska läkartidningen*, April 18, 1958) used cycloserine combined with isoniazid to treat 19 patients with pulmonary tuberculosis. Serving as controls were 23 similar patients who were given a combination of PAS with isoniazid. The two groups were compared with respect to temperature, weight, sedimentation rate, and roentgenographic and bacteriological findings. With the exception of one patient in the control group, there was a rapid fall of the temperature to normal. The sedimentation rate showed marked improvement in both groups, but the roentgenographically demonstrable improvement was definitely better in the cycloserine-treated group than in the controls. A dosage of 0.5 Gm. of cycloserine was well tolerated.

Group Treatment of Alcoholics.—Since February, 1957, a clinic for alcoholics in Linköping has held group discussions for 30 of its patients. G. Wretmark and co-workers (*Svenska läkartidningen*, April 11, 1958) reported that the patients were carefully selected for this treatment, excluding those with mental deterioration, severe personality abnormalities, flaccid or mythomanic characteristics, or serious criminal tendencies. Qualifying for this treatment were depressive, dysphoric, tense, sensitive, aggressive, explosive, and hysteroid alcoholics. At a meeting, the attendance should include at least four and preferably five or six patients with a physician bereft of the paraphernalia of his calling and on his guard not to slip into didactic speech likely to encourage silence on the part of the others. The patient of a domineering turn of mind has to learn not to monopolize the conversation. Meetings attended by too many patients tended to become useless. Meetings were also held for the wives of alcoholics. The follow-up account of how these patients fared showed among other things that only two were not carrying out normal work. There were, however, five who discontinued this treatment at an early stage.

UNITED KINGDOM

Stokes-Adams Syndrome Treated with ACTH.—On the assumption that heart block in Stokes-Adams syndrome might be due to inflammation of the bundle of His, Litchfield and co-workers (*Lancet* 1:935, 1958) treated three patients with this condition with ACTH. An infective or rheumatic origin was suspected in each case. The attacks had previously failed to respond to atropine and adrenergic drugs. In two patients the attacks ceased, with reversion of the electrocardiogram to normal in one. In the third patient the attacks ceased on the day ACTH was given, but they recurred when the dose was reduced. The development of heart failure in this patient necessitated a reduction in the dosage of ACTH. Complete heart block then developed, and the patient died about four months later. Although the prognosis in Stokes-Adams syndrome is unpredictable, it was thought that the improvement in these patients was not due to chance recovery. It is possible that the improvement may not have been due to the suppression of inflammation but to an alteration in the metabolism of the heart muscle. An autopsy on the fatal case showed a cellular reaction with secondary calcification extending across the bundle of His from the diseased aortic valve.

Osteoarthritis.—Ross and co-workers (*Brit. M. J.* 1:1040, 1958) injected 0.1 to 0.3 ml. of 5% benzyl salicylate and 5% camphor in peanut oil into knee joints in 53 patients with osteoarthritis at weekly intervals for six weeks. In addition 18 patients, under light general anesthesia, received an intraosseous injection of 25 to 40 ml. of a solution containing 0.2% salicylic acid and 1% sodium citrate in water in the subcortical areas of the femur and a like amount in the tibia. The patients were followed up for six months after the injections, and an estimate was made of function; of the patient's own assessment of the value of the treatment; and of any change in such physical signs as heat, tenderness, effusion into the joint, and range of movement. Some improvement was observed in 76%. This was graded as excellent in 27%, good in 30%, and fair in 19%. The authors do not believe that the improvement was due to a simple local analgesic effect, as it did not occur until at least 24 hours after the injection and was usually not noticed until after the third or fourth injection.

Routine Medical Checkups.—Although routine medical examinations or health checks are common in the United States they are not in Great Britain, except for those exposed to special industrial or occupational hazards. The value of such checks has recently been questioned in *The Times*. A member of Parliament asked whether public money should be spent by the British Broadcasting Corporation on routine health checks for its senior executives. The Chairman of the B. B. C. replied that the cost involved was a relatively small premium to pay for the maintenance of the health of key personnel. Several well-known physicians then joined in the correspondence, stating that they considered routine examinations of this type virtually useless in the early detection and treatment of disease.

Lancet supported this view. It admitted that sometimes such a periodic health check might be useful but that its advantages are exaggerated. Few disorders can be detected before symptoms appear, with the possible exceptions of diabetes and tuberculosis. Acute conditions may strike down healthy people before symptoms appear, while in many chronic disorders treatment can be given equally well in the later stages of the disease. Such examinations if made routinely would add 280 million dollars a year to the cost of the National Health Service, a sum that might be used more effectively in other ways. Another argument against periodic health checks is that they would create anxiety and neurosis in certain persons. Such examinations are likely to be of value only when a large organization employs a full-time physician to examine personnel at fairly short intervals. He would then be expected, like the general practitioner, to know their social, medical, and occupational backgrounds.

Dental Erosion Caused by Soft Fruit Drinks and Ices.—Mellanby and co-workers (*British Dental J.* **104**:305 [May 6] 1958) stated that soft fruit drinks, carbonated beverages, fresh fruit juices, candies known as "acid drops," and frozen synthetic fruit drinks sold as "iced lollies" cause dental erosion. Carbonated beverages are less harmful than the others. Most of the observations were carried out on the teeth of rats and dogs, but some were made on extracted human teeth. Many children suck iced lollies for long periods, and in this way citric or tartaric acid comes in direct contact with the teeth for long periods, causing marked erosion. Sucking fruit-flavored candies, which also contain these acids, is also harmful to the teeth.

Secretion of Hydrocortisone.—Hydrocortisone is one of the major steroids secreted by the adrenal cortex, and measurement of its rate of production is a valuable index of adrenal activity. The need for a simple method of estimating its production by the body led Cope and Black (*Brit. M. J.* **1**:1020, 1958) to explore the possibility of using hydrocortisone labeled with radioactive carbon (C^{14}) for this purpose. The principle of the estimation is the well-established one of isotope dilution. If a small amount of C^{14}-labeled hydrocortisone is introduced into the body it may be expected to be metabolized in the same manner as the endogenous hydrocortisone, with which it becomes diluted. It can be estimated in the urine by means of its radioactivity. The activity of a 24-hour collection of urine is measured and compared with the original activity of the ingested hydrocortisone. From the data obtained Cope and Black calculated that the average daily excretion of hydrocortisone is about 13.5 mg. in normal persons, with a range of 5 to 28 mg. In six subjects with severe but nonendocrine disease, the mean daily excretion was 20 mg. The response to routine ACTH therapy was variable, the highest output being 257 and the lowest 21.8 mg. daily, a figure within the normal unstimulated range. In paients with hepatic cirrhosis the excretion rate was slow, and in hyperthyroidism it was high. In hypoadrenalism due to adrenal cortical hypofunction or to hypopituitarism hydrocortisone production was between 0.6 and 1.2 mg. daily with a mean of 0.9 mg. When the activity of the adrenals was inhibited by therapy with prednisone or 9-α-fludrocortisone therapy the excretion fell to 2.3 mg. daily. A hydrocortisone production of only 1 mg. daily was found in a pseudohermaphrodite, confirming the belief that a low output occurs in such patients.

New Gastric Antisecretory Agent.—Douthwaite and Hunt (*Brit. M. J.* **1**:1030, 1958) used the new antisecretory agent, Nacton, or (1-methyl-2-pyrrolidyl) methyl benzilate methyl methosulfate, to reduce the gastric secretion of patients with peptic ulcers. This compound has an atropine-like action of long duration and reduces the gastric secretion of hydrochloric acid in response to a test meal without appreciable side-effects. The changes in the gastric secretion of acid were studied in 23 patients with duodenal ulcer and two with gastric ulcer. The stomach was washed out while the patient was fasting, and a 750-ml. test meal containing 50 Gm. of glucose per liter and a dye not absorbed from the stomach was given. After 30 minutes the gastric contents were recovered, the completeness of recovery being checked by washing out the stomach. From the amount and composition of the dye remaining in the gastric contents the amount of the latter that had passed into the duodenum was found, together with the total amounts of acid, chloride, and pepsin secreted. It was then possible to describe the gastric secretion of acid in terms of milliliters of 0.16 N hydrochloric acid, the concentration at which it is produced by the parietal cells. The dose of drug given was that which did not produce side-effects. Initially a dose of 8 to 10 mg. a day was given in divided doses every six hours, and this was increased by 4 mg. daily until side-effects were produced. The dose was then reduced until these just disappeared. Given every six hours, Nacton effected a continuous reduction of gastric secretion to about 50% of the control value in response to a test meal. In patients with marked hypersecretion the inhibition was often greater when expressed as a percentage of the control than in those with lower levels of secretion. There was little change in the rate of gastric emptying and no change in the mean output of gastric nonparietal secretions.

MISCELLANY

SALUTE TO THE MEDICAL PROFESSION

Alex Dreier

Men . . . and medicine. This combination has inspired great thoughts and deeds for 4,000 years, and spells a brighter, healthier future for every human being on earth. Men of purpose, ideals, and highly refined skills . . . general practitioners, radiologists, pathologists, internists, psychiatrists, surgeons, hospital administrators, public health officers, obstetricians, orthopedists, pediatricians. Men like your family doctor—who knows you better than you know yourself.

These are the kinds of men who are the human fabric of the American Medical Association—dedicated to the promotion of "the science and art of medicine and the betterment of public health." And this they have done, to the benefit of all.

To most people A. M. A. is simply a familiar group of letters. "Something to do with doctors" is the pat explanation. Well, it does have something to do with doctors, all right—and with lawyers and bankers and bandits and movie queens and the people next door.

It was born under dramatic circumstances back in 1847 in Philadelphia. There, determined physicians from 22 states met to discuss the inferior quality of medical education in the United States, the disappointingly brisk traffic in harmful patent medicines, and the lack of a recognized code of ethics. These things they discussed, and many more. And from their deliberations came the national association of physicians known as the American Medical Association—a democratic association of more than 70,000 physicians welded into almost 2,000 county and district medical societies. Physicians from all 48 states and Hawaii, Alaska, Puerto Rico, the Isthmus of Panama, and the District of Columbia. A big, busy organization with its own national legislative body, which includes delegates from the Army, Navy, and Air Force, the Veterans Administration, and the Public Health Service.

The A. M. A. works through its councils, bureaus, departments, and committees. It is concerned with everything you can think of, and dozens of things you may not: education, chemistry, nutrition, rehabilitation, industrial and rural health and research, medical motion pictures, publications, and pesticides.

The A. M. A. performs so many services, both seemingly simple and deceivingly complex, that it would be futile to attempt to enumerate them here. But what does it do for the public? What, as the man says, is in it for me?

First of all, it promotes health. It produces films on health, and cooperates in both local and network radio and television programs concerned with health and better living.

Through newspapers, magazines, and other media the Association's public relations department produces authentic health news and issues a widely used weekly news release, as well as huge quantities of special releases concerning the association's annual and clinical sessions. A staff cooperates with writers of all media in collecting medical literature, checking references, and arranging interviews with medical authorities.

It also publishes books, pamphlets, booklets, special reports, and the widely read magazine *Today's Health*. And it answers questions—endless questions on an endless variety of health problems. As many as 15,000 letters annually pour into its Health Education Bureau, out of the almost 24,000 letters that inundate staff employees at A. M. A. headquarters in Chicago each week.

It even maintains a Bureau of Investigation, a sort of medical F. B. I., without actual police powers but with a highly effective organization to probe the thousands of complaints involving the unscientific side of medicine. Law enforcement agencies have frequently used this bureau's information and files to crack down on quacks. Other specialized councils or committees examine food and cosmetics and drugs and devices of all kinds, insuring their purity, effectiveness, and safety.

And the Association also maintains inspection and consultation services for medical schools and hospitals, resulting in a tremendous upgrading of standards, better-trained physicians, and higher-quality medical care for the American people.

Out of the wealth of bills introduced on medical subjects, the A. M. A. selects and supports those with primary medical implications, the promise of real benefit to the public. It also throws its considerable support and prestige behind measures it considers essential to the well-being of the nation as a whole—backing food and drug laws, hospital construction acts, and bills supporting the United States Public Health Service, for example.

Yesterday's physician carried a small black bag containing a half-dozen instruments to take care of your ills. Today's physician keeps a well-equipped office embellished with modern, complex mechanical and electronic aids. He also uses the great facilities of modern hospitals and laboratories. And most of all, despite the busiest era in the history of modern medicine, he continues to educate himself. Don't ask us where he finds the time or how—we cannot imagine. We know only that he does, somehow, find the minutes and hours to digest a wide variety of pamphlets, books, reports, articles, and

From "America on the Go" broadcast over NBC-Monitor, Sunday, June 22, 1958, 6:05 p. m. EST.

958
167

medical magazines and journals. He can't possibly know everything about medicine, but he keeps trying! And because he does, the American physician is the most respected member of the world medical profession today.

There must be other reasons—and there are. We are fortunate indeed to live in what some like to call the "Golden Age of Medicine"—and golden it is. The experts estimate that more than a million and a quarter Americans are alive today because of new treatments developed in the last 10 years. In any previous period of history, they would have died. But thanks to modern medical science, and the dedicated men who breathe life into it, they are alive and well. Just 10 years ago life expectancy was 65 years. Today it is pushing into the lower 70's.

And it is a fact, an almost unbelievable one, that three out of four prescriptions written today could not have been written before World War II, because the drugs they call for simply didn't exist! This is progress, fantastic progress!

Working together, the doctor and the medical research specialist have combined their talents and skills to knock the props from under pneumonia, once a major killer of mankind.

And the scourge of poliomyelitis could be virtually wiped out today, if enough people would simply obtain the required number of inoculations. Tuberculosis is gasping on the ropes, thanks to modern medicine with its inspired techniques. And waiting for the knockout blow are rheumatic fever, kidney disorders, influenza, and venereal diseases. It will come—when enough money and enough time can be spent to wage the kind of fight it takes to lick man's most feared ills.

Cancer? A terrible, super-efficient killer, perhaps the most feared of all man's ailments. But cancer can be, and has been, cured in its early stages. Some day there will be a vaccine to prevent it.

America, 1958, a year of great progress and the promise of even more in the future. A time of wonder drugs, miracle-like vaccines, unique therapies. And a time of test and experiment and discovery in the never-ending search to wipe out the physical and mental evils to which man falls heir. Medical science is so efficient today it has created problems for the political scientist by making man so healthy that, if he follows the rules, he finds himself in a sort of geriatric isolation from the mainstream of the economy. The numbers of healthy oldsters are growing each day. Soon a large segment of the population will be in the over-65 group, thanks to the never-ending efforts of the medical researchers.

Yesterday we talked of stomach flu and cod liver oil and aspirin. Today it is steroids, broad-spectrum antibiotics, and radioactive materials. Perhaps the most-talked-of drugs of all are the tranquilizers. Millions have used them; some have abused them. But in the hands of a competent physician, they have been wonderful aids in certain specific cases. Death from childbirth has been practically wiped out, thanks to new knowledge and new techniques developed by the men who refused to allow the status quo to remain, to be accepted as the "natural thing."

Medical progress is spectacular and dramatic. Influenza death rates have declined 91% since World War II; tuberculosis, 77%; active rheumatic fever, 76%; maternal deaths, 77%.

But to the medical men, what we call the present is the past. For them the future must be now. Now is when they must defeat cancer and other painful, killing, and crippling diseases. For despite all the progress, there remains much to be accomplished. Heart disease and mental disorders are still our greatest medical problems. And heart disease and cancer alone account for 900,000 American deaths each year. These and many other problems will be discussed beginning tomorrow during the A. M. A. Annual Session in San Francisco.

In the next decade, some experts predict that as many as 3 or 4 million lives will be saved, thanks to new medicine and new techniques. And in the forefront of the battle will be the physician and surgeon, the researcher, the country doctor, and the North Michigan Avenue specialist—not creating just a better America, but better Americans, through medical science.

MEDICAL FILM REVIEWS

Children with Cleft Palates: A Program of Speech Development: 16 mm., color, sound, showing time 29 minutes. Produced in 1956 by and procurable on rental ($5) or purchase ($160) from University of Michigan Audio Visual Education Center, Ann Arbor, Mich.

The purpose of this film is to illustrate the procedures which should be followed to encourage the development of good speech in children with cleft lip and palate. It provides a general outline of treatment in relation to the age and developmental growth periods of children. It also demonstrates the objectives of the various specialists concerned with care of the child and the atmosphere in which the stimulation of speech can best take place. It outlines the comprehensive long-term care necessary for the patient with a congenital defect, and it is an up-to-date review of modern total care of these patients. The moving x-ray scenes, models, and other such features are excellent. This is an outstanding film which should provide inspiration and encouragement to the parents and the patient. It is medically and technically correct and is recommended highly for showing to parents, patients, teachers of exceptional children, physicians, and dentists.

MEDICAL LITERATURE ABSTRACTS

INTERNAL MEDICINE

The Treatment of Hypertensive Heart Failure and of Hypertensive Cardiac Overload by Blood Pressure Reduction. F. H. Smirk, M. Hamilton, A. E. Doyle and E. G. McQueen. Am. J. Cardiol. 1:143-153 (Feb.) 1958 [New York].

The introduction of ganglion blocking agents provided an effective method of reducing blood pressure and of maintaining the blood pressure of patients with hypertension at, or near, normal levels. It has been demonstrated that reduction of blood pressure alone, without the use of digitalis, mercurial diuretics, or salt restriction, is sufficient to relieve the symptoms of hypertensive heart failure. The authors report their experience in the treatment of 310 patients with hypertensive heart failure with ganglion blocking agents—hexamethonium bromide initially, and latterly pentolinium (Ansolysen), chlorisondamine (Ecolid), and mecamylamine (Inversine). It is of fundamental importance that the systolic blood pressure, in the trough of the blood pressure fall, should be decreased to between 120 and 135 mm. Hg. At this level of systolic blood pressure the diastolic blood pressure will also be satisfactory. Many of the less satisfactory results obtained by the authors were in patients in whom side-effects made it impracticable to reduce the cardiac overload to this extent. The patients were followed for periods of between 2 and 7½ years.

There were 4 groups of patients. In the first group, of 41 patients with left ventricular failure only, 35 were controlled without recourse to digitalis, mercurial diuretics, or salt restriction. Thirteen of these patients have died. In the second group, of 44 patients with combined heart failure, 38 of whom also had attacks of nocturnal dyspnea, 20 were relieved without ancillary measures. Of this group, 22 have died so far. Thus, 35 of the 85 patients with heart failure have died. The average duration of treatment of those who have survived is 50 months, and the duration of treatment of those who died was 23 months. Forty of the 50 surviving heart-failure patients are able to work.

The third group comprised 127 patients who had dyspnea on exertion but no failure. Four of these patients later died of heart failure. In addition, there were 26 other deaths, including 12 from cerebral vascular accidents, 7 from cardiac infarction, 5 from uremia, and 2 from various other causes. The fourth group of 98 patients had neither failure nor dyspnea but had moderate to severe hypertension. In this group 5 patients died of congestive failure. In addition, there were 26 other deaths, including 15 from cerebral vascular accidents, 3 from cardiac infarction, 5 from uremia, and 3 from other causes. The authors conclude that in hypertensive patients heart failure results more from cardiac overload, rather than from irreversible muscle damage, and that it can be prevented or controlled solely by measures to reduce the blood pressure.

Chronic Myocarditis. S. Van Creveld and H. A. P. Hartog. Nederl. tijdschr. geneesk. 102:211-215 (Feb. 1) 1958 (In Dutch) [Amsterdam].

The authors present the histories of 3 patients, a 25-year-old man, a 9-year-old boy, and a 40-year-old woman, who died of cardiac decompensation resulting from chronic myocarditis. In the course of years interstitial myocarditis developed, with extensive fibrosis of the heart muscle. One patient presented a syndrome suggestive of constrictive pericarditis. The authors cite several literature reports on cardiac dilatation and decompensation caused by chronic myocarditis. In some of these reports, as in the patients here presented, there were no signs of endocarditis or pericarditis. The histological picture did not resemble that of rheumatic myocarditis. Resistance of the cardiac decompensation to all therapeutic measures has also been described previously, and it has been suggested that a virus infection might be the cause.

Antibacterial Therapy of Pulmonary Tuberculosis. F. V. Shebanov, V. S. Gavrilenko, T. F. Smurova and V. N. Adamovich. Sovet. med. 21:58-63 (No. 12) 1957 (In Russian) [Moscow].

Shebanov and his associates state that treatment of active pulmonary tuberculosis must be carried out in a hospital so as to make possible administration of antibacterial drugs, collapse therapy, or surgical procedures. Hospital treatment for 3 to 4

The place of publication of the periodicals appears in brackets preceding each abstract.

Periodicals on file in the Library of the American Medical Association may be borrowed by members of the Association or its student organization and by individuals in continental United States or Canada who subscribe to its scientific periodicals. Requests for periodicals should be addressed "Library, American Medical Association." Periodical files cover 1949 to date only, and no photoduplication services are available. No charge is made to members, but the fee for others is 15 cents in stamps for each item. Only three periodicals may be borrowed at one time, and they must not be kept longer than five days. Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

months is to be followed by treatment in a sanatorium for 7 to 10 months. After the patient has been discharged from the sanatorium, the administration of antibacterial drugs is continued for 3 to 6 months. Reversal of primary progressive tuberculosis requires about 2½ years. Treatment of primary tuberculosis in its infiltrating phase is commenced with a combination of streptomycin and PAS. To avoid the development of streptomycin resistance, this drug after 2 months is replaced by phtivazid, which after being given for the next 2 to 3 months is followed by 1 to 2 months' courses of streptomycin in combination with either phtivazid or PAS for the next 6 months. The entire course of treatment of an adult patient requires 120 Gm. of streptomycin, 240 Gm. of phtivazid, and 3,600 Gm. of PAS.

Tuberculous lymph nodes are treated for 1½ to 2 years with the administration of the 3 antibacterial drugs, streptomycin, PAS, and phtivazid, by interrupted courses. Acute miliary tuberculosis requires the combined administration of the 3 drugs for the first 3 months. The treatment is continued for 10 to 12 months. Acute limited destruction of pulmonary tissue requires 1 to 2 months of treatment with streptomycin and PAS to be followed by artificial pneumothorax if the process is not terminated. This is to be followed by treatment for 3 to 4 months with phtivazid and PAS. In caseous pneumonia the authors resort to combined treatment with streptomycin, phtivazid, and PAS administered for 3 to 4 months. Further treatment is continued for 4 to 5 months with phtivazid combined with PAS. This is followed by interrupted courses with streptomycin and PAS. This therapy diminishes the toxicity and aids in the transition of the process into the chronic, fibrous, cavernous tuberculosis. The duration of treatment of caseous pneumonia is from 1 to 2 years. A number of patients with fibrous, cavernous tuberculosis require radical surgical treatment. Surgical interventions are preceded by treatment with streptomycin and PAS.

The effect of the antibacterial drugs upon the chronic types of pulmonary tuberculosis, especially those of the cavernous type, is sometimes ineffective. For such cases the authors advise tuberculin therapy and repeated transfusions of small amounts of blood. Tuberculin is given subcutaneously, beginning with a small dose which is increased by 0.1 to 0.2 cc. every 5 to 6 days until 12 to 15 injections have been given in the course of 2 to 3 months. Tuberculin therapy is particularly indicated in cases of long-continued infiltrative and focal tuberculosis with continued intoxication, hilar infiltrates, and cirrhotic process with some destruction and involvement of peripheral lymph nodes. Transfusions of 30 to 50 cc. of blood once a week are performed 8 to 12 times. Blood transfusion is particularly indicated in exudative pleurisy and in serous and purulent pleuritis. The introduction of antibacterial therapy in the treatment of pulmonary tuberculosis has not completely solved the question of treatment of cavities. Complete closure of cavities is observed rather rarely with this type of therapy. Recurrences develop 1 and 2 years after treatment. The employment of pneumothorax in combination with antibacterial therapy increases the percentage of positive results.

The Intradermal Test in Tularaemia with Particular Reference to the Reaction Elicited in Regions of Different Incidence of the Disease. O. Ljung. Acta med. scandinav. **160:**135-147 (No. 2) 1958 (In English) [Stockholm].

The investigations described were undertaken to investigate the test with Pasteurella tularensis antigen and to obtain a definition for the positive reaction that would establish whether tularemia infection has definitely occurred. To judge from the literature and the author's own experience, persons with manifest tularemia always seem to present a clearly positive reaction. The study also included observations of the intradermal test in other classes of subjects. The intradermal test with antigen consisting of chemically inactivated Pasteurella tularensis was performed on 3,211 persons. A dose of 0.1 ml. was administered intracutaneously on the volar aspect of the forearm. Of the persons tested, 40 had had manifest tularemia 2 to 21 years previously (mean, 7½ years). The other persons had never been known to have the disease. They were from areas with different incidences of tularemia. Reactions to the intradermal test ranged from completely negative to strongly positive, with areas of edema of mean diameter up to 100 mm. The reaction was read at 72 hours. A positive reaction was defined as one in which there was an area of edema with a mean diameter of 7 mm. or, if vesicles or pustules were present, at least 5 mm. A lower criterion for a positive reaction would result in nonspecific reactions falling in this class.

Of the 40 patients who had had tularemia 2 to 21 years previously, 36 (90%) gave positive responses. Of 131 tests on hospital patients from areas where tularemia was unknown, none was positive. It is evident from this that the intradermal test is a fairly reliable means of demonstrating past infection and that nonspecific positive reactions are rare. In 472 hospital patients from areas with a low incidence of tularemia, 7 positive reactions were found (1.5%). Of 2,047 persons from areas where there was a high incidence of the disease, 227 (11.1%) gave a positive reaction. There was no difference in the type of the positive reaction in those who had had tularemia and those who had not, although, as a rule, the former presented a stronger reaction. However, of the 17 persons with the largest areas of edema, 10 had not, as far as they were aware, had tularemia. These positive reactions must be ascribed to atypical, abortive, or

symptomless tularemia. According to the literature, nonspecific reactions have not been observed. Through some error in the preparation of the test solution, however, several patients in the 2 last series had strong nonspecific reactions. When 432 (76.2%) of 567 subjects gave positive reactions, further study showed that these reactions were due to an irritant in the dilution medium and not to the inactivated Pasteurella tularensis.

Intradermal and Agglutination Tests in Tularaemia, with Particular Regard to the Demonstration of Past Infection. O. Ljung. Acta med. scandinav. **160:**149-154 (No. 2) 1958 (In English) [Stockholm].

The investigations in the preceding paper had shown that 90% of persons who had had tularemia 2 to 21 years previously gave a positive response for the intradermal test. When the agglutination test was performed on 36 of these patients, 6 exhibited negative agglutination reactions. Of 151 subjects with no history of tularemia but with positive intradermal reactions to killed Pasteurella tularensis antigen, only 47 exhibited positive agglutination tests. As previous studies by the author have shown, it appears likely that these 151 persons had previously had an atypical, abortive, or asymptomatic attack of tularemia. The high proportion of negative agglutination reactions in these persons was unexpected. Simultaneous intradermal and agglutination tests were performed on 104 consecutive hospital patients who, although they had no history of tularemia, were from an area where there was such infection. Twelve persons gave a positive intradermal test. In only 2 cases was a positive agglutination reaction (and a positive intradermal reaction) elicited. These reactions do not show parallelism, and occasionally one may find positive agglutination reactions and negative intradermal reactions, but, on the whole, the intradermal test appears to be the better for demonstrating past tularemia. The intradermal test with killed Pasteurella tularensis seldom appears to give rise to positive agglutination reactions to this antigen. Ninety-two subjects still gave a negative agglutination reaction 4 to 9 weeks after an intradermal test.

Kidney Biopsy in Acute Glomerulonephritis. C. Brun, H. Gormsen, T. Hilden and others. Acta med. scandinav. **160:**155-163 (No. 2) 1958 (In English) [Stockholm].

Aspiration biopsies were performed on 13 patients with glomerulonephritis. Judging from the case histories and the clinical findings, all the patients were considered to have acute glomerulonephritis. Seven cases were severe, the 24-hour endogenous creatinine clearance ranging between 0 and 3 ml. per minute. At biopsy all the patients but 1 showed severe changes, all the glomeruli being uniformly and severely damaged. These 6 patients died during the acute stage. One patient had a few glomeruli with some intact capillary loops; this patient was treated with dialysis but died 9 months later. Six cases were mild, the 24-hour endogenous creatinine clearance varying between 46 and 116 ml. per minute. Correspondingly, the changes seen at biopsy were moderate. All 6 patients recovered. On the basis of the criteria generally accepted in evaluating the pathological changes in glomerulonephritis, the histological pictures observed in the biopsies were considered subchronic or chronic changes in many of the patients. This discrepancy between clinical and histological pictures might be due to the fact that some of the patients had acute exacerbations in a chronic disease. This possibility could, however, be excluded in at least 1 of the patients. Another explanation is that the histological changes in the glomeruli were considered of older standing than they actually were. As the technique of kidney biopsy provides the possibility of seeing the earliest stages of the acute disease, the concept of the histological picture at these stages might have to be revised.

Prevalence, Nature and Identification of Leukocyte Antibodies. J. L. Tullis. New England J. Med. **258:**569-578 (March 20) 1958 [Boston].

Increasing awareness of the role of autoimmune mechanisms in the production of certain types of idiopathic hemolytic anemia and thrombopenic purpura has stimulated work on the possible relation of idiopathic leukopenia to autoantibody formation. As a first step in large-scale identification of naturally occurring leukocyte antibodies, it was deemed necessary to develop a reliable test. Such a test is described. The effects of mixtures of normal leukocytes and heterologous leukocyte serums (rabbit antihuman white blood cell serums) were observed. The constant findings in such mixtures were decreased motility of the neutrophils, agglutination, and, in the more potent antiserums, hyper-Brownian movement and lysis. If the ameboid motility of the cells was quantitated, it was possible to calculate the decrease in absolute numbers of viable (motile) cells during the test period. For the purposes of this study, an arbitrary standard, the lysis index, was defined as the product of percentage decrease in white blood cell count times the percentage decrease in motile forms. The resulting empiric values gave a marked difference between normal and pathological serum. A lysis index (60-minutes percentage decrease in white blood cell count times 60-minute percentage decrease in ameboid forms) between 0 and 25 was established as representing a normal serum. The index for normal serum averaged 4. Abnormal serums showed an average decreased white blood cell count of 23% at 30 minutes and 35% at 60 minutes plus a decreased ameboid motility of 18%

at 60 minutes. The average lysis index of 70 strongly positive serums averaged 100 times as great as that of the negative serums. The range of positive values varied between 165 and 2,184, with an average of 630.

A total of 132 serums from leukopenic patients and 102 from persons without leukopenia but with various blood dyscrasias and hepatosplenic diseases, such as leukemia, cirrhosis, infectious hepatitis, anemia, and purpura, were tested for the presence of leukocyte agglutinins. Antileukocytic activity was demonstrated in serums from patients with a wide variety of hematological diseases with leukopenia; it was found in a large proportion of serums from patients with leukopenia with a hyperplastic bone marrow and in none from patients with leukopenia with a hypoplastic bone marrow. Specificity of this antileukocytic activity could be demonstrated by its complete absorption from positive serum by leukocyte suspensions, but not by suspensions of erythrocytes or thrombocytes. In persons with leukopenia exhibiting positive antileukocytic tests in whom clinical improvement took place, antileukocytic activity disappeared from the serum coincidentally. Chemical and electrophoretic study showed that antileukocyte-antibody activity is made up of at least 2 components, 1 having the characteristcs of a beta globulin and 1 having the characteristics of an alpha globulin.

The Pathogenesis of the Hepatorenal Syndrome. N. A. Lassen and A. C. Thomsen. Acta med. scandinav. **160**:165-173 (No. 2) 1958 (In English [Stockholm].

Acute renal failure as a complication of liver or biliary tract disease has been designated the "hepatorenal syndrome." This paper is concerned with the pathogenetic factors of the hepatorenal syndrome. A clinical series comprising 30 patients, in all of whom acute renal failure developed as a complication of liver or biliary tract disease, was analyzed. Two-thirds of the patients had been in a state of shock with arterial hypotension when the renal failure started. Clinical information concerning the remaining patients was often somewhat meager. It is possible, however, that some of these patients had been in a state of incipient shock, a suggestion supported by the demonstration of marked water and electrolyte depletion in several patients. The clinical course of the renal disease and the histological examinations of the kidneys demonstrated a striking similarity between the acute renal disease complicating liver or biliary tract disease and the acute renal disease initiated by shock. It is concluded that the renal disturbance in the hepatorenal syndrome is not caused by a mysterious nephrotoxin but more likely by renal hypoxia due to manifest or incipient shock. The clinical implications of this pathogenetic concept are discussed. Emphasis is put on the recognition and treatment of the often atypical shock which initiates this dangerous and not too uncommon renal disease.

Carcinoma of Pancreas and of Periampullar Region. J. Solis and A. A. Hernández Andoanegui. Rev. invest. clin. **9**:591-610 (Oct.-Dec.) 1957 (In Spanish) [Mexico, D. F.].

Forty-two patients with primary carcinoma of the pancreas or of the region of the ampulla of Vater were observed at the Hospital de Enfermedades de la Nutricíon, of Mexico City, during the years from 1947 to 1955. Most of the patients of both sexes were between the ages of 50 and 60 years. Carcinoma involved the pancreas in 32 cases and the ampullar region in 10. The tumor was located in the head of the pancreas in 26 cases, at either the body or the tail in 6 cases, about the ampulla of Vater in 6 cases, and in the lower third of the common bile duct in 4 cases. Jaundice, epigastric pain, pruritus, and rapid loss of weight were the predominant symptoms. They were more severe in patients with pancreatic carcinoma than in those with periampullar carcinoma. Abdominal palpation revealed hepatomegaly in 21 cases, a palpable gallbladder in 6 cases, and a nodular, hard, fixed, epigastric mass (which was interpreted as a pancreatic tumor) in 8 cases. In 75% of the cases the direct bilirubinemia and the alkaline phosphatase value of the blood were increased and the prothrombin time prolonged. In 27% there was a hyperglycemia with curves of the diabetic type. Roentgenologic examination of the gastroduodenal region showed definite shadows of a pancreatic tumor in 7 cases. The average lapse of time between appearance of symptoms and first consultation was 3 months in patients with periampullar carcinoma and 4½ months in patients with pancreatic carcinoma.

All the patients were subjected to operation. Preoperatively, the prothrombin time, liver insufficiency, diabetes mellitus, anemia, and poor nutrition were controlled. Antibiotics were given only if symptoms of cholangitis were present. None of the 32 patients with primary carcinoma of the pancreas was at the operable stage when they reported for the first time for consultation. They had either distant metastases or diffuse lesions of carcinoma and fixation of the tumor structure to the upper mesenteric blood vessels and/or to the portal vein, as seen on exploration. Twenty-seven patients in this group had palliative surgical treatment, which caused improvement in pruritus and in biliary obstruction to a certain degree. The operative mortality was 37%. Ten patients had only an exploratory laparotomy for the purposes of confirming the clinical diagnosis and of giving indications or contraindications for radical operation. Five pa-

tients with periampullar primary carcinoma underwent pancreatoduodenal resection. Two of these patients died of metastases 6 and 18 months, after the operation. Three patients are living and are in good state of health. One of the patients has lived more than 5 years since the operation. The other 2 patients have lived 2 years and 5 months, respectively, since the operation.

Polycythemia Vera: Study of Coagulation Abnormalities, Both Thrombotic and Hemorrhagic. S. J. Wilson, H. E. Heath and W. E. Larsen. J. Kansas M. Soc. **58**:90-92 (March) 1958 [Topeka].

The coexistence of hemorrhage and thrombosis in polycythemia vera is a paradox. In the active phase of the disease there is an increase in the red blood cell mass, hematocrit, platelets, and viscosity, all of which produces a thrombotic tendency. At the same time, however, the prothrombin and the fibrinogen value are at least relatively decreased per unit volume of whole blood, and this contributes to a hemorrhagic tendency. In an attempt to explain this paradox, comparative observations were made on 37 normal adult men and women, 23 patients with polycythemia vera who were in good clinical control, and 7 patients with polycythemia who had received no treatment. Answers were sought to 3 specific questions, prompted by the description in recent works of a peculiar form of clot retraction with red blood cell release in patients with polycythemia vera: 1. Is the fibrinogen value actually decreased? 2. Is there an increase in fibrinolysis, and is the red blood cell fall-out phenomenon related to fibrinolysis? 3. Is the phenomenon of red blood cell fall-out corrected by therapeutic control of the polycythemic state? The study revealed that hematocrit readings in the treated patients were essentially within normal limits. There was no difference between the fibrinogen values of normal subjects and those of treated patients with polycythemia vera. Fibrinolysis was also essentially the same except in 2 treated patients. A tremendous difference, however, was found in the red blood cell fall-out phenomenon. In 39.5% of the treated patients, the fall-out phenomenon was still abnormal (3 to 4+). The untreated patients had excellent values of fibrinogen. It must be remembered that fibrinogen is measured in milligrams per 100 cc. of plasma, not of whole blood; therefore, with high hematocrit readings there is a relative decrease in fibrinogen value. All but 2 of the untreated patients had a 4+ red blood cell fall-out phenomenon. Fibrinolysis was not increased except in 1 patient in whom there was complete lysis. Increased fibrinolysis, then, which was observed in 3 patients only does not explain the fall-out phenomenon. The inability of the fibrin clot to hold red blood cells (resulting in the fall-out phenomenon) was striking in untreated polycythemia vera. Therapy did not correct this defect, and this suggests a deficiency in the fibrin itself and possibly in its precursor fibrinogen. The extremely poor fibrin strands probably contribute to the hemorrhagic tendency.

Appendicitis of the Aged. M. Bourreau. Rev. prat. **8**:395-405 (Feb. 1) 1958 (In French) [Paris].

Appendicitis should no longer be regarded as a rare condition in the aged. Recent advances in therapy have improved the prognosis in general, but in individual cases the outcome is still unpredictable. The clinical manifestations of the disease in elderly patients differ little from those usually found in adults. The symptoms presented by the aged are often, however, less striking than those of younger patients, and experience, patience, and thoroughness of examination are required for their recognition. Early examination, in the initial stages of the disease, greatly facilitates the establishment of the correct diagnosis. The evolutional, occlusive, and pseudotumoral aspects, the real origin of which is not always easy to determine, are usually the result of a delay in consultation or of an inadequate diagnosis at the outset—circumstances largely responsible for the gravity of the prognosis in the aged. Severity, rather than certain alleged clinical aspects that have no real specificity, is the essential mark of appendicitis in patients over 60 years of age. The statistics in a favorable series covering the period 1943-1954 showed 8 deaths in 1,508 cases in patients aged 59 years or less (0.53%) as compared with 6 deaths in 58 cases in patients aged 60 or more (10.2%). The value of early diagnosis and prompt intervention is shown by the following mortality rates: 0% when the operation was performed on the first day; 44% when it was performed on the second day; and 50% when it was performed after the third day.

Immediate operation whenever an acute attack of appendicitis is diagnosed during the first few hours is, therefore, just as essential in the aged as in children and younger adults. Medical treatment alone, when the disease is not recognized until it has resulted in the formation of an inflammatory mass, may lead to a complete regression of the lesions. The patient should be closely watched, however, so that action can be taken at the first clinical and hematological signs of abscess formation. Operation should always be preceded by at least a few hours of preparation, which may be more or less extensive according to the condition of the patient. General anesthesia, secured with a minimum of the anesthetic drug to insure perfect oxygenation, is usually well tolerated even by patients of advanced age. The operation should be performed with the most careful attention to detail. The postoperative course in favorable cases is generally smooth, but the lessened recuperative powers

of the aged may lead to a longer convalescence than usual. Unexpected failures, with complications and possibly death, may, however, occur even in apparently favorable cases.

Exfoliative Cytology of Gastric Carcinoma. R. O. K. Schade. Brit. M. J. 1:743-744 (March 29) 1958 [London].

In an attempt to achieve earlier diagnosis of carcinoma of the stomach, while the tumor is still confined to the mucosa, 2,500 gastric cytological examinations were performed. Lavage with 100-200 cc. of sodium chloride or Ringer's solution was used for obtaining cell material. Twenty-five cases were discovered by this method, in which other investigations by x-ray and gastroscopy were negative. The best material for cytology was obtained from those patients in whom the malignant lesion was subsequently found to be small, often confined to the mucosa. Paradoxically, the material most difficult to interpret comes from those patients in whom the tumors are large and widely ulcerated. The lavage fluid of these cases contains much debris and many organisms and inflammatory cells which make cytodiagnosis difficult or impossible. Patients with an achlorhydria which is always associated with structural mucosal changes, such as a diffuse chronic atrophic gastritis, should be investigated until it has been proved that there is no evidence of carcinoma. Cytological examination, to which few patients object, is an easy method for screening and following up. The gastric cellular material reflects better than any other method the pathological processes of the entire gastric mucosa and can provide satisfactory diagnostic results which compare favorably with radiologic and gastroscopic findings.

Serum Glutamic Oxaloacetic Transaminase, Lactic Dehydrogenase, and Glutamic Pyruvic Transaminase Activity in Evaluation of Heart Muscle Damage. J. S. La Due. Am. J. Cardiol. 1:308-314 (March) 1958 [New York].

Myocardial infarction was produced in dogs by the injection of plastic spheres into the coronary sinus. In every experiment the serum glutamic oxaloacetic transaminase (SGO-T) activity rose promptly with peak levels appearing 9 to 23 hours after infarction. Fifteen infarcts, produced in dogs by tightening a ligature 10 days after it had been placed about a coronary artery, were all associated with an increase in the SGO-T activity. Both the height and the duration of increased enzyme activity appeared to be proportional to the size of the infarct. In similar experiments on 7 dogs in which infarcts were produced, the SGO-T activity increased 3 to 10 times, the serum glutamic pyruvic transaminase (SGP-T) activity increased 3 to 5 times, and the serum lactic dehydrogenase (SLD) activity increased 2 to 3 times over the normal.

Serums obtained within 12 to 48 hours after the onset of unequivocal acute transmural myocardial infarction and daily thereafter in 300 patients were anaylzed for SGO-T activity. In all but 3 patients when the serum was obtained at the time of acute infarction, the SGO-T activity rose 2 to 20 times over the normal within the first 48 hours. The height and the duration of the increased SGO-T activity appeared to be roughly proportional to the size of the infarct as estimated electrocardiographically. Secondary elevations of SGO-T activity were seen after recurrent chest pain caused by the extension of the infarction or the occurrence of a new infarction in the same patient. In 10 patients with acute transmural myocardial infarction, in whom the activity of all 3 enzymes in the serum was studied, the SGO-T activity increased 2 to 20 times over the normal, the SLD 2 to 10 times over the normal, and the SGP-T 1 to 3 times over the normal. No correlation was found between the SGO-T activity and the white blood cell count, the erythrocyte sedimentation rate, the presence or absence of shock, the absolute levels of the blood pressure, the presence of heart failure, the location of the infarction, or the use of anticoagulant drugs.

The SGO-T activity was studied in 50 patients with coronary insufficiency whose electrocardiograms showed evidence of ischemia, as manifested by moderate to marked T-wave inversion sometimes associated with ST-segment changes but without Q-wave abnormalities. The SGO-T activity remained within normal limits in 34 of these patients despite the persistence of prolonged substernal pain. The SGO-T activity rose in 16 of the 50 patients, suggesting acute heart muscle cell damage. In 8 patients pain had been present for 3 to 6 days before the SGO-T activity increased. Angina pectoris or coronary insufficiency is not associated with a rise in SGO-T, SLD, and SGP-T activity unless it is presumably accompanied by heart muscle cell damage. The SGO-T activity in patients with acute rheumatic fever without carditis was not elevated. In some, but not all, patients with extensive rheumatic carditis, the SGO-T activity was increased. The SGO-T activity was followed during the course of pulmonary infarction in 7 patients and remained normal in all but 1 patient whose peak enzyme activity was 80 units.

The SGO-T test is of diagnostic value as a specific index of the presence and size of acute heart muscle cell necrosis. SGO-T activity has proved particularly useful in deciding whether acute heart muscle cell damage has occurred when chest pain, like that seen with myocardial infarction, develops in patients with equivocal electrocardiographic changes. In such patients, if the SGO-T activity is carefully followed throughout the duration of pain

and for 4 to 12 days thereafter, many patients may be saved weeks of invalidism or anticoagulant therapy may be instituted to prevent impending infarction. Acute myocardial damage must be presumed to be present in patients with chest pain and equivocal electrocardiographic changes, who have increased SGO-T activity in the absence of known active liver disease. The SGO-T activity will usually help distinguish acute pericarditis and pulmonary infarction from acute myocardial infarction. Further study is needed to evaluate the significance of alterations of SGO-T activity in patients with acute rheumatic carditis.

Porphyria: Report of Nine Cases Diagnosed in the Greater Hartford Area, Including a Family with three affected Members. M. J. Seide. New England J. Med. **258**:630-635 (March 27) 1958 [Boston].

Two patients died of acute intermittent porphyria within a 6-month period in hospitals of the Greater Hartford area. To determine the frequency with which this diagnosis has been made, all cases coded as porphyria were pulled from the record rooms of several hospitals located in the Greater Hartford area. A total of 9 cases (4 of them previously reported) were found and are presented in this paper, together with a brief review of the pertinent literature.

Two main groups of porphyria are recognized. One, porphyria erythropoietica, is inherited as a Mendelian recessive; it is characterized early in life by photosensitivity, reddish teeth, red urine, increased hemolysis, increased erythropoiesis, excessive and abnormal porphyrin formation in bone, and splenomegaly. The urine contains increased amounts of uroporphyrins, small amounts of coproporphyrins, but no porphobilinogen. Porphyria hepatica, the other main group, is so named because abnormal porphyrins are believed to be formed in the liver. Acute intermittent porphyria is the most common subgroup. Individual attacks may be long or short. The patient has abdominal pain, peripheral neuropathy, and mental disturbances, with any or all of the following signs and symptoms: hypertension, dilated pupils, attenuation of retinal arterioles, tachycardia, restlessness, cold and clammy extremities, steady or colicky abdominal pain, intestinal spasm, decreased peristalsis, obstipation, urinary retention, or cremasteric spasm. Another subgroup, porphyria cutanea tarda, is often confused with porphyria erythropoietica. However, this form usually begins in the 4th or the 5th decade of life. Photosensitivity, skin pigmentation, and hepatic dysfunction are present; the urine is red, zinc porphyrin is present, and liver porphyrin is increased. Porphyria cutanea tarda is a chronic disease. Death is due to liver failure. There are usually no abdominal or neurological manifestations.

The term "mixed porphyria" describes cases with symptoms of both porphyria cutanea tarda and acute intermittent porphyria, which may or may not appear simultaneously. Latent porphyria is most commonly found in relatives of patients with acute intermittent porphyria. The heredity of acute intermittent porphyria is as a Mendelian dominant, not sex-linked. Several affected families have been reported, and cases 7, 8, and 9 of this report concern a sister, a brother, and their mother. The mother of the 2 siblings had died in 1936. The weight of evidence that she had porphyria is overwhelming, but if her 2 children had not died and if no one had searched the microfilmed files for her record, this case would have remained recorded as "chronic salpingitis and encephalomyelitis." Porphyria is seldom diagnosed unless it is considered. Signs and symptoms are protean. The diagnosis depends on urine tests. Every patient admitted with abdominal pain, bizarre nervous system disease, or psychiatric difficulties should be examined for acute intermittent porphyria, and a specimen of his urine should be allowed to stand exposed. Factors considered to be "precipitating factors" may be early symptoms. Treatment is symptomatic and supportive. Many cases of porphyria, especially mild ones, are overlooked. Even in the 4 severe cases reported in this paper, all terminating fatally, the diagnosis was missed on several previous admissions.

Considerations on Therapy and Prognosis of Recent Myocardial Infarction. B. Jasiński. Schweiz. med. Wchnschr. **88**:264-269 (March 15) 1958 (In German) [Basel, Switzerland].

The author reports on 58 women and 86 men, between the ages of 30 and 80 years, with recent myocardial infarction, who were treated at the medical clinic of the Canton Hospital in Winterthur, Switzerland, between 1950 and 1957. Of the 144 patients, 73 died, a mortality rate of 50.5%; the myocardial infarction itself was the cause of death in 35, pulmonary infarction in 15, and cardiac insufficiency in 23. Eighteen of the patients had diabetes mellitus, 21 had hypertension, 8 had chronic disease of the kidneys, 2 had cirrhosis of the liver, and 31 had previously suffered damage to, or insufficiency of, the myocardium as a result of coronary arteriosclerosis with or without hypertension. Of the 144 patients, 30 were in bad condition on admission, with shock, pulmonary edema, and gallop rhythm, and 24 of these died within the first 3 days after admission; if one excludes these patients with a particularly unfavorable prognosis, 114 remain, and 43 of these died, representing a mortality rate of 37.7%. Of the 114 patients, 66 were given anticoagulant therapy, and 48 did not receive anticoagulants. Thirty-two (66.6%) of the 48 patients died, and 12 (18.2%) of the 66 patients died. Dangerous complications, such as pulmonary in-

farctions and peripheral arterial emboli, occurred already within the first and the second week after the myocardial infarction. Of the patients treated with an anticoagulant, only 4 had these complications, while 27 of those who did not receive anticoagulant therapy had such complications. With the help of an early-instituted anticoagulant therapy, it is possible to bridge this dangerous period.

The author believes that all patients with myocardial infarctions—except those with the well-known contraindications, including peptic ulcer, cirrhosis of the liver, and hemorrhagic diathesis—should be treated with anticoagulants, irrespective of whether they are to be considered as good or bad risks. Of the 58 women reported on, 57 were over 50 years of age, while of the 86 men, 12 were between the ages of 30 and 50 years. These data show that myocardial infarction occurs at an earlier age in men than in women. The risk of myocardial infarction in women coincides with the approaching menopause, and that in an abrupt way and without those fluent transitions by which the time of the occurrence of myocardial infarction is characterized in men. The coincidence with the menopause partly seems to be the result of a reduced estrogen production.

A group of 40 patients, 28 men and 12 women, with myocardial infarction were treated with a proprietary preparation of protein-free animal heart muscle extract (Recosen). Thirty-one patients, 20 men and 11 women, who did not receive Recosen served as controls. Although the course of the electrocardiograms did not differ in these 2 groups, the clinical course of the patients treated with Recosen was less eventful, particularly because of the damping effect of the drug on the extrasystoles. Only 3 of the 40 patients required glyceryl trinitrate for more than 10 days, as compared with 8 of the 31 patients. In addition to the well-known coronary dilator effect of Recosen, this drug exerts a direct influence on the metabolism of the myocardium, as was shown with the aid of the isotope technique (radioactive vitamin B_{12}). Recosen is a valuable adjuvant in the treatment and after-treatment of myocardial infarction.

Diagnosis of Atherosclerosis: I. Correlation Between Clinical Diagnosis, Serum Cholesterol and Low-Density Lipoproteins, and Resting and Exercise Electrocardiograms. H. Engelberg. Am. J. Cardiol. 1:315-322 (March) 1958 [New York].

Serum cholesterol determinations and ultracentrifugal determinations of low-density lipoprotein levels shown as atherogenic index values were performed on, and electrocardiograms and ballistocardiograms at rest and after a double 2-step exercise test according to Master's criteria were obtained from, 560 adult patients, between the ages of 21 and over 61 years, in private practice. There were 149 patients with a history of old myocardial infarction and 349 patients with no clinical evidence of severe coronary, peripheral, or cerebral atherosclerotic disease. Of the 149 patients, 103 were men and 46 were women, and of the 349 patients, 260 were men and 89 were women. In the group without evidence of atherosclerotic disease up to the age of 50 years, the serum cholesterol level did not differ significantly between the sexes, whereas the atherogenic index was significantly lower in women, thus paralleling the known lower incidence of atherosclerosis in women before the menopause. Patients with a history of myocardial infarction had significantly elevated lipid levels at all ages. Although the serum cholesterol and atherogenic index values were usually parallel, when the lipid parameters were divergent, the lipoprotein determination was more accurate than the serum cholesterol determination as related to the clinical diagnosis. The serum cholesterol and lipoprotein values were high in 27 patients in whom peripheral atherosclerotic disease was the presenting illness. In 100 patients with hypertension, the average lipid values were significantly elevated in those patients who had experienced a coronary or a cerebral incident. The lipid measurements correlated directly and significantly with the severity of the electrocardiographic findings at rest and after exercise. The combined application of the various tests will frequently aid in the earlier diagnosis of atherosclerotic disease and in the selective application of prophylactic measures.

Autogenous Vaccine in Prophylaxis of the Common Cold. J. M. Ritchie. Lancet 1:615-618 (March 22) 1958 [London].

The author, director of a public health laboratory in Birkenhead, England, had given over a period of 20 years autogenous vaccines against colds to 60 or 70 persons who requested such treatment. Although no special investigations were possible, it gradually became apparent that almost the only failures occurred in some cases of long standing, where it was practically certain that degenerative changes had taken place in the mucous membrane. In a few cases the improvement might be explained on psychological grounds, but the series was becoming too long for this explanation to be sufficient. As a result of these and other findings, the opinion was formed that the common cold might be due to 2 factors—the virus, whose function is essentially depressive, and an invasion by the patient's own normal but heterogenous secondary organisms, which are usually present in a state of equilibrium, overstepping the mark only as a result of the patient's depressed resistance caused by the virus. If this explanation is correct, these volunteers, experiencing the prodromal stage for a day or 2, kept on

catching cold as far as the virus was concerned, but they were immunized against the effects of their own organisms.

In the winter of 1955-1956, studies were made on 184 volunteers; 109 were given weekly injections of autogenous vaccines from their own nasopharyngeal flora and 75 were given carbol saline only. The number of volunteers continuing the vaccine injections was 109 for each of the first 2 months, and 51 for each of the next 3—i. e., a total of 371 volunteer-months for the whole period. The corresponding figure for the controls was a constant 75 for each month—i. e., a total of 375 volunteer-months. In the vaccinated there were 13 full colds in the 371 volunteer-months as against 77 in 375 volunteer-months in the controls. The cold rate per month for the controls was 5 times that of those who were vaccinated throughout the course. The rate of absence from work through "colds" and "upper respiratory infections" was also greater in the controls.

Antibiotics in Small Doses for the Common Cold. J. M. Ritchie. Lancet **1**:618-621 (March 22) 1958 [London].

Although the author had encouraging experiences with autogenous vaccines in the combat of the common cold, he feels that mass vaccine treatment is impracticable. He decided to try a controlled short-term antibiotic therapy after ascertaining the sensitivity of the patient's pharyngeal flora before the winter began. If vaccines had given a degree of active immunity, then suitable antibiotic tablets, given at the beginning of the prodromal stage, might well give sufficient passive protection by depressing the pharyngeal flora temporarily to correspond to the depression of the patient's resistance. To avoid risk of producing insensitive strains of bacteria or of disturbing permanently the balance normally maintained between patient and pharyngeal flora, the author decided to try the effect of brief local application only. After preliminary trials had shown that the sucking of lozenges did reduce the number of pharyngeal flora but that this effect was temporary, invitations to cooperate were sent to some of the larger works in the neighborhood.

Studies were made on 919 volunteers from October, 1956, to April, 1957. These were divided into 2 groups; 581 volunteers received short-term antibiotic treatment when they felt a cold beginning, and 338 received an inert tablet. In the treated group, the number of prodromal stages reported was 287 (49%), of which 22 (7%) went on to full colds. In the control group, the prodromal stages numbered 182 (54%), of which 87 (48%) went on to full colds—i. e., 4 colds per 100 volunteers in the treated and 26 per 100 in the control group. The figures for adults were 2.6 colds per 100 volunteers and 23.1 colds per 100 controls respectively. The small dosage of antibiotics used had no permanent effect on the sensitivity of the pharyngeal bacteria or on the proportions of the various species. Some volunteers had irritation of the throat and tongue. It is suggested that, after sensitivity tests have been done, a controlled stort-term antibiotic therapy can, without risk, drastically cut down the effects of the common cold. This method can easily be applied in industry by any well-staffed medical center cooperating with a laboratory.

Antihistaminic "Protective" Sera, Applied to the Treatment of Asthma and Other Syndromes Termed Allergic. R. Benda. Presse méd. **66**:455-457 (March 15) 1958 (In French) [Paris].

Certain human serums possess the property of protecting the guinea pig against the toxic action of histamine. This fact, which was established by the author and his co-worker Urquia in investigations that began in 1947, applies in principle only to serums that are spontaneously protective as the result of a natural and constant antihistaminic resistance. On the other hand, a greater or less lack of protective potency in the serum, as well as possible variations, characterizes a particular terrain designated as asthmogenic or, more commonly, allergic in patients with various allergic conditions. These essentially experimental data have given rise to a new therapeutic concept, which is to reproduce in patients with asthma or other allergic diseases the state of antihistaminic protection obtained in the guinea pig with a single injection of protective serum. Spontaneously protective serums are hard to get, since they are found only in 10% of even apparently healthy donors. Inactive serums, however, may in various circumstances acquire (or recover) all or part of the antihistaminic properties in which they are deficient. The acquired antihistaminic properties of serum are particularly noticeable when they develop under the influence of favorable medical treatment, regardless of its kind. The protective power of the serum was calculated in 100 patients with asthma who were subjected to various treatments (injection of protective serum, of deltacortisone, and of protective serum in association with deltacortisone). In 59 of 76 patients who showed an undeniable clinical improvement, there was an evident increase in the coefficient of protection (p), so that p exceeded 70 in 21 patients and even reached 100 in 2. Only serums with a p value equal to or higher than 70 should be regarded as protective; a p value between 40 and 70 provides relative protection, and a p value between 10 and 40 gives only a hint of protection.

Good results of variable duration were obtained in about 70% of 2,393 patients with asthma, usually by a single subcutaneous injection of 2 cc. of protective serum (children under 5 years of age were given only 1 cc.). The beneficial effects lasted in

most of the patients from 6 months to 1 year; some of the patients had no recurrence for 3, 4, or 6 years; others again were protected only for a few weeks or for 2 or 3 months. In such cases a second and even a third injection of protective serum may be given; the second injection is frequently much less effective than the first and should be considered merely as a preparation for the third injection, which generally gives much more definite and lasting results. An interval of at least 2 months should elapse between two consecutive injections. This interval may be prolonged without inconvenience. Side-effects, such as an increase in temperature lasting one day, mild headache, dizziness, transient nausea, and more often the recurrence of dyspneic phenomena lasting a few hours, sometimes occurred but were rare. The administration of delta-cortisone combined with the serum, in very small doses and discontinuously, makes it possible to wait for the more or less rapid, usually lasting effect of serotherapy, serving as a relay for the hormone treatment which is always hard to manage.

The use of protective serum should apparently be extended to all the diseases (eczema, urticaria, migraine, etc.) in which the protective power of the patient's serum is reduced or lost, as it is in asthma. Caution, however, should probably be exercised in the presence of certain associations, such as asthma and eczema, whether the two syndromes coexist or whether they occur alternately at more or less brief intervals, because although a single injection of protective serum may lead to the simultaneous disappearance of both skin and respiratory disorders in some patients, in others one condition may be improved while the other is made worse.

The Reproductive Characteristics of Diabetic Men. D. Babbott, A. Rubin and S. J. Ginsburg. Diabetes 7:33-35 (Jan.-Feb.) 1958 [New York].

One hundred sixty-seven married men with diabetes mellitus were chosen at random from 2 outpatient diabetes clinics. They were interviewed with respect to their reproductive histories. The data were compared with those obtained by similarly interviewing a control population selected at random from among married nondiabetic men attending an outpatient dental clinic. The diabetic men's wives had a significantly higher incidence of abortions than did those of the control population. The incidence of abortion among the wives of the diabetic men before and after the clinical recognition of the husbands' diabetes did not differ significantly. The diabetic group did not differ significantly from the control population with respect to number of conceptions, premature births, stillbirths, live births, sex ratio of offspring, or birth weights of offspring. Thus, no evidence was found to support the thesis that the children of diabetic men differ discernibly at birth from those of normal men.

SURGERY

Intracranial Eradication of Middle Cerebral Aneurysms. H. H. Gass, J. F. McGuire and D. R. Simmons. J. Neurosurg. 15:223-236 (March) 1958 [Springfield, Ill.].

The authors gained a favorable impression in regard to direct eradication of middle cerebral aneurysms. Their report is based upon experience with 12 craniotomies for 12 middle cerebral aneurysms occurring in 10 patients. There were 2 deaths, the first representing an error in selection and the second an error in management. The survivors are neurologically intact except 1 patient with a mild aphasia. In 2 patients multiple aneurysms were present, the first requiring 3 craniotomies for 3 separate middle cerebral aneurysms and the second requiring 1 craniotomy for a middle cerebral aneurysm and an anterior communicating aneurysm. In both of these patients all aneurysms were eradicated, and they are neurologically intact. This report deals chiefly with aneurysms arising from the distal portion of the middle cerebral artery. It is this group the authors stress as being especially amenable to intracranial clipping. Fortunately, the distal portion probably represents the most common site of origin for middle cerebral aneurysms. Although a good result was obtained in a single instance of an aneurysm arising from the proximal portion of the main trunk of the middle cerebral artery, this is insufficient experience for drawing any conclusions. Such lesions also are probably too medial to be reached easily by opening the fissure and may possibly best be reached via a subfrontal approach by following the internal carotid artery out to the bifurcation into the middle and anterior cerebral arteries.

Complications Related to Mitral Commissurotomy: A Study of 500 Operations. J. Lenegre, B. Coblentz and L. Sprovieri. Minerva chir. 13:95-103 (Jan. 31) 1958 (In Italian) [Turin, Italy].

The authors review the complications which have developed in some of the 500 patients who underwent mitral commissurotomy between 1951 and 1957. Anatomic alterations of the left atrium and of the mitral valve consisted in thrombosis of the left auricular appendix in 57 patients, in valvular calcification in 126, and in mitral insufficiency in others. Surgical operation caused worsening of a preexisting mitral insufficiency in 97 patients, in most of whom a mild reflux occurred. Massive reflux was fatal and occurred in 6 patients only. Ventricular fibrillation and cardiac arrest developed in 16 patients, 5 of whom died during the operation and 1 died immediately after the operation of cerebral anoxia; heart beat was restored in 9 patients. Arterial embolisms were observed in 11 patients (2.2%); 5 of these embolisms were cerebral (1 fa-

tal), 2 appeared in the femoral artery, 2 appeared in the aortic bifurcation (1 fatal), and 2 were simultaneously cerebral and peripheral. Preoperative anticoagulant treatment appears to be the best prophylactic procedure for embolism. It should be given to all patients undergoing mitral commissurotomy, who have previously had episodes of auricular fibrillation.

Auricular fibrillation, which was the most frequent and the most benign postoperative complication, occurred in 62 patients and was corrected in 53. Acute pulmonary edema and right ventricular insufficiency were related to an incomplete surgical operation, which was, in turn, due to adverse anatomicocardiac condition. Two patients with pulmonary edema and 3 patients with ventricular insufficiency died. Hemopericardium, which occurred in 10 patients, was corrected by puncture. An evident pulmonary embolism appeared in 9 patients, causing death in 2. To anticipate embolism, besides the anticoagulant treatment, femoral veins were ligated in 4 patients. Thirty-nine patients (7.8%) died at operation or in the immediate postoperative period. The most frequent causes of death were circulatory collapse (6 patients), cerebral and aortic-bifurcation embolism (6), and rupture of the valves, pillars, and tendons (6). Postoperative joint and chest pain, accompanied by fever, which some workers call "postmitral commissurotomy syndrome," was observed in 25 patients (5%). A 3-month prophylactic treatment for this disorder consisted in the administration of long-acting penicillin, combined with aspirin, and in elimination of all possible foci of local infection. Respiratory symptoms, on the basis of which the original mitral commissurotomy was performed, reappeared in 11 patients; only in 2 of them was it possible to ascertain the inefficacy of the original mitral commissurotomy.

Results of Surgical Treatment of Coarctation of the Aorta: Records from the Clinic of Prof. P. Santy. P. Marion. Lyon chir. **54**:242-248 (March) 1958 (In French) [Paris].

Santy's records show that from 1948 to 1957 he operated on 120 patients with coarctation of the aorta. Six patients died within 1 month after the operation; 1 died 3½ years later, possibly of a ruptured aneurysm; and 7 were lost to follow-up. Satisfactory long-term results were obtained in 80% of the remaining 106 patients; in 18% the circulatory conditions were improved; and in only 2% did the operation fail to produce functional improvement. These results, added to others reported in the world literature, especially those of Crafoord, show the advisability of early routine operation in patients with coarctation of the aorta.

Certain technical principles adhered to in these cases may well be pointed out. Santy, like Crafoord, believes (1) that insofar as possible all existing anastomoses should be preserved and that, in particular, no intercostal artery should be sacrificed, and (2) that an effort should always be made to complete the resection with an end-to-end anastomosis to avoid the need for a graft or an atypical anastomosis. The two methods by which these objectives may be attained are extensive freeing of the aorta and the use of controlled hypotension. The extensive freeing of the aorta is essential for success; only when the dissection is carried well above and below the coarctation will it be possible to bring the two segments of the aorta together. The use of controlled hypotension in adult patients with hypertensive forms of coarctation facilitates the dissection, gives suppleness to the vessels, and makes it possible to bring the two segments together without difficulty. Trimethaphan camphorsulfonate (Arfonad), the ganglionoplegic used, is easily manageable and fleeting in its effect, and no particular complications were caused by its use. The period of controlled hypotension was limited to the intrathoracic vascular stage of the operation, the parietal stage being carried out while the tension was normal. The incidence of hemorrhagic complications has been no higher since the use of ganglionoplegics began than it was before.

Intracranial Internal Carotid Artery Aneurysms: Results of Treatment by Cervical Carotid Artery Ligation. H. A. Shenkin, P. Polakoff and B. E. Finneson. J. Neurosurg. **15**:183-191 (March) 1958 [Springfield, Ill.].

The controversy as to whether cervical carotid artery ligation alone or an intracranial procedure is preferable in treatment of intracranial aneurysms of the carotid artery seems to have been resolved in favor of the latter by the majority of those who recently have expressed opinions on this problem. The authors, however, present a series of 19 consecutive patients treated only by cervical carotid artery ligation to show that this method of treatment is an adequate one for intracranial aneurysms of the internal carotid artery. The 19 patients were 24 to 70 years of age, the average age being 47½ years. Eighteen of the patients had a subarachnoid hemorrhage as a cause for hospitalization. On admission, 3 patients were semicomatose and 4 were considered to be in moderate distress, being mentally obtunded and exhibiting evidence of hemiparesis in addition to symptoms of subarachnoid hemorrhage. The remainder of the patients were conscious and oriented. All the patients except 1, who died, were fully conscious at the time of ligation. Eight aneurysms were located at or near the origin of the posterior communicating artery, 5 were located at the bifurcation of the internal carotid artery, and 5 were located between these sites. One patient had multiple intracranial aneurysms of 1 internal carotid artery below its bifurcation.

Arteriography was generally delayed until the patient was conscious. An average of 12 days elapsed between onset of hemorrhage and arteriography. Ligation of the carotid vessels was done shortly after arteriography, frequently the same day. In 8 patients arteriography was performed via the patent carotid artery 1 week to 1½ years after ligation. In no instance was the involved carotid vessel or the aneurysm visualized. Ligation of a carotid vessel was generally accomplished by lightly ligating the vessel so as to approximate the intima without crushing it and then firmly and tightly ligating the vessel proximal to this first ligature. It was hoped to reduce the possibilities of a propagating thrombus developing. The ligation was done with the patient under local anesthesia, and the patient was observed for development of focal neurological signs over a period of 20 to 30 minutes while the artery was occluded and before the wound was closed. A second principle of ligation was to prevent collateral circulation through the external carotid vessel, and therefore the internal carotid artery itself was primarily or secondarily closed off or else the external carotid artery was ligated together with the common carotid artery.

Eighteen of the 19 patients have survived from 6 months to 7½ years after operation (an average of 3⅛ years) without evidence of recurrent hemorrhage. There was 1 immediate postoperative death, and 1 patient is permanently incapacitated with a hemiplegia. Seventeen patients are economically useful. There were 6 postoperative hemiplagias, of which 3 cleared completely and 2 have improved sufficiently for the patients to work. From these results, and a review of the literature, it appears at this time that there is no necessity of attacking this type of aneurysm intracranially. Ligation of the internal carotid artery at an interval after ligation of the common carotid artery appears to be safest as regards prevention of morbidity. The age of the patient at the time of ligation does not seem to influence morbidity.

Results of Surgical Treatment of Pulmonary Stenosis (Blalock-Taussig, Potts, and Brock Operations): Records from the Surgical Clinic of Prof. P. Santy. P. Marion. Lyon chir. 54:254-267 (March) 1958 (In French) [Paris].

The records of the Centre Lyonnais for cardiovascular surgery show that up to July 1, 1957, operations performed on patients with stenosis of the pulmonary artery numbered 386, 350 of which form the basis for this discussion. The mortality was high: 86 (24%) of the patients died, 65 at the hospital within 1 month after the operation and the remaining 21 some months or years later. Chronic anoxia, which usually prompts the operation, is the most frequent cause of peroperative and postoperative failure. Cardiorespiratory syncope, the form under which it appears during the operation, occurred in 18 patients, most of whom were highly cyanotic before the operation. Cerebral anoxia, or cerebral thrombosis, the form in which chronic anoxia manifests itself after operation, may assume various clinical aspects, e. g., coma, or hemiplegia or monoplegia or aphasia with or without coma.

Brock's orificial valvulotomy was performed on 28 patients with pulmonary stenosis without interventricular communication. Four patients died, 1 of peroperative syncope, 1 of thrombosis of the right ventricle, 1, a 52-year-old woman, of cardiorespiratory insufficiency, and 1 of anoxia. This last patient was a nursling who was found at autopsy to have a suborificial stenosis which had not been detected at exploration. Follow-up of the 16 surviving patients with electrocardiographic signs of tight stenosis before operation showed perfect or good late results in 13 and functional failure in 3. There were no late deaths.

The operations used in treating patients with the tetralogy of Fallot with permeable pulmonary stenosis, i. e., the ordinary type, were those of Potts (158), Blalock (95), and Brock (10). The operative risk is greater when the aorta is on the right side. Potts's operation is safer than Blalock's, especially in patients aged less than 1 year or more than 15 years. The late results, however, were about the same (80 to 90% good) for both of these operations. Acute postoperative cardiac insufficiency is exceptional; it was never seen after operations for the tetralogy of Fallot but appeared only in patients with more complex forms of pulmonary stenosis. Infectious endocarditis developed in 6 patients after the Blalock operation, but in only 1 after the Potts operation. The results of the Blalock-Taussig and Potts shunts in patients with rare forms of pulmonary stenosis (extreme tetralogy of Fallot, pseudotruncus arteriosus, and tricuspid atresia) were generally poor. The dimensions of the foramen ovale and the age of the patient seem to be the controlling factors in cases of tricuspid atresia. Patients in whom pulmonary stenosis is accompanied by excessive deviation of the electric axis constitute a special group with a particularly poor operative prognosis, as shown by 14 deaths in 22 cases. The fact that the 8 survivors were much older at the time of the operation than those who died seems to show that the risk diminishes with age and that the operation should not be performed too soon.

Clinical Management of Posttraumatic Rupture of the Thoracic Aorta. B. Eiseman and W. G. Rainer. J. Thoracic Surg. 35:347-358 (March) 1958 [St. Louis].

The authors report on 6 men, between the ages of 20 and 63 years, with rupture of the thoracic aorta due to nonpenetrating trauma. The 1st pa-

tient had an aneurysm of the thoracic aorta after a severe injury to the chest sustained in an automobile accident; the aneurysm was located immediately below the left subclavian artery and was followed by chest roentgenograms without evidence of its progression for 16 years. The 2nd patient had a post-traumatic aneurysm which was first observed 2 years after injury and raised the clinical problem of its resection against the advisability of watchful waiting. The latter method was chosen, and the lesion remained unchanged for 4 years. For 9 days after injuries sustained in an automobile accident, the 3rd patient had essentially no symptoms referable to the chest. He was about to be discharged when within an 8-hour period chest pain occurred which was associated with hemothorax. The patient went into shock, and an emergency thoracotomy on the left revealed a ruptured aneurysm of the thoracic aorta which was resected. A nylon graft was inserted, but the patient died shortly after the occluding aortic clamps were removed. After severe injury to the chest, which the 4th patient sustained in a fall from a third-story window during an epileptic seizure, the chest roentgenogram showed widening of the mediastinum. Exploratory thoracotomy revealed diffuse periaortic hematoma, but no evidence of rupture of the aorta was found. Three weeks after the injury and negative exploratory thoracotomy, a chest roentgenogram revealed an aortic aneurysm immediately beneath the left subclavian artery. Thirteen years after chest injury sustained by the 5th patient, an aneurysm of the descending thoracic aorta was thought to be enlarging and producing back and chest pain localized to this region. It was successfully excised and replaced with a homograft, providing relief of symptoms. The 6th patient sustained severe trauma to the left side of the chest at the age of 17 years when he was kicked by a mule. A mass was noted in the descending portion of the aortic arch on a chest roentgenogram taken 38 years after the injury. A follow-up by serial roentgenograms was carried out for 9 years, and marked enlargement of the aneurysm was observed during the last 4 years, 43 years after the injury.

The findings in these patients and observations made by other workers in 95 cases of post-traumatic rupture of the thoracic aorta collected from the literature suggest the following clinical approach. Early thoracotomy should be performed if incomplete laceration of the aorta is seriously suspected. Such a procedure should include careful inspection and palpation of the entire length and circumference of the thoracic aorta for evidence of laceration. Exploratory aortotomy may even be necessary to visualize the site of rupture if no other method discloses the origin of diffuse periaortic ecchymosis. An asymptomatic period of 2 to 3 weeks may elapse after severe injury of the chest before delayed rupture of the aorta occurs. Immediately before the exsanguinating hemorrhage from an incomplete laceration of the aorta or from the resulting aneurysm, there commonly is a short period (1 to 36 hours) of lesser leak. This premonitory warning must be recognized instantly, and immediate thoracotomy must be performed for operative cure. Asymptomatic post-traumatic aneurysms of the thoracic aorta, discovered incidentally more than 1 month after injury, probably will stabilize and can be managed expectantly with serial roentgenograms of the chest at 6-month intervals. Should there be any evidence of enlargement or development of symptoms, the aneurysms should be excised and replaced with a suitable graft.

Primary Extragenital Chorioepithelioma in the Male Mediastinum. G. J. Magovern and B. Blades. J. Thoracic Surg. 35:378-383 (March) 1958 [St. Louis].

The authors report a case of primary extragenital, mediastinal chorioepithelioma in a 20-year-old man who was admitted to the George Washington University Hospital in Washington, D. C., because of a radiopaque shadow in the hilar region on the right, revealed for the first time by a routine chest roentgenogram taken 2 months before admission. The patient was asymptomatic except for occasional pain in the left side of the posterior chest wall. A right-sided thoracotomy was performed, and a large globular, irregular, encapsulated mass was removed from the anterior superior mediastinum. Microscopic examination of the surgical specimen revealed a germinal tumor, the prime elements of which were seminoma and embryonal carcinoma, with areas of choriocarcinoma. Serial sectioning of both testes was negative for germinal tumor but did show azoospermia. Gynecomastia was not present. The remainder of the patient's clinical course was rapidly downhill because of extensive skeletal and retroperitoneal metastasis. He died 5 months after the surgical removal of the tumor.

The case of this patient is believed to be the 25th reported case of primary extragenital chorioepithelioma in a male patient proved by autopsy and serial sectioning of both testes. It is the 10th such case of mediastinal origin. Although extragenital primary tumors have been considered in the past to be the result of aberrations in somatic development, other workers recently have shown by comparative morphogenesis the germinal cell development of extragenital primary tumors as well as of genital primary tumors. While most cases are reported as "extragenital chorioepithelioma," they are, in reality, cases of germinal tumors in which chorioepithelomatous elements have developed, and it is questionable whether these cases should be reported as a distinct entity. The hormonal elaboration, the age of the patients, and the pres-

ence of gynecomastia (in 12 of the 24 patients whose cases were collected from the literature) have been briefly discussed and stressed as diagnostic criteria in these patients. The treatment of chorioepithelioma, which is highly radioresistant, consists of radical excision and is extremely unsatisfactory. Most patients die rapidly of metastasis.

Successes and Failures in Homografting of Arteries. D. Erlik. Harefuah **54**:113-116 (March 2) 1958 (In Hebrew with English Summary) [Tel Aviv, Israel].

Of the various indications for arterial surgery, the most important are aortic aneurysm, obliteration of the aortic bifurcation (Leriche's syndrome), arteriosclerotic obliteration of the iliac or femoral arteries, and some rare cases of thromboangiitis obliterans (Buerger's disease) in which the obliteration involves the femoral or even the iliac arteries. The exact diagnosis is important, because a deficient outflow below the graft dooms the operation to failure from the start. To obtain an exact picture of the arterial tree, translumbar aortography was used. The procedure was performed on 103 patients by injecting a 70% iodopyracet (Diodrast) solution, with the patient under anesthesia, without a single serious complication. Freeze-dried lyophilized grafts were used. The cases of 10 patients are described in detail. Two of these patients were advanced in years and had aneurysms; they were operated on with good result, as revealed by follow-up for 6 and 15 months respectively. Of 3 patients who underwent aortic resection and received homografts for obliteration of the aortic bifurcation, 1 was a therapeutic failure because of deficient outflow, 1 who was followed up for 6 months obtained excellent results, and 1 obtained good results as revealed by follow-up for 5 months. Homografting of peripheral arteries was carried out in the remaining 5 patients. Relatively short grafts of 20 to 25 cm. in length were used in 3 of these patients, who obtained lasting good results as revealed by follow-up for 13 months. The homografts used in the remaining 2 patients were 42 cm. in length. One patient was a therapeutic failure due to thrombosis. Good results were obtained and maintained for 16 months in the last patient. In general, the shorter the grafts, the better the results. Careful selection of patients and exact technique are the prerequisites for good and lasting results.

Malignant Transformation of Gastric Adenomatous Polypi. D. Rosenberg and J. A. de Mello Saraiva. Rev. paulista med. **52**:1-16. (Jan.) 1958 (In Portuguese [São Paulo, Brazil].

Gastric adenomatous polyp is a rare, proliferating, benign tumor prone to undergo malignant degeneration. It is more common in men and in persons between the ages of 60 and 70 years. As a rule, it is asymptomatic, or it may cause symptoms resembling those of gastric or duodenal ulcer, gastric cancer, or other gastric disorders. Pernicious anemia, atrophic gastritis, and massive gastric or rectal hemorrhages are frequent. A diagnosis is made by roentgenologic examination of the stomach and the esophagus and confirmed by gastroscopy. The treatment consists of either polypectomy or gastrectomy, according to the number and size of the polyps.

The subjects of this report were a woman and a man, 37 and 59 years old respectively. The first patient had symptoms of gastroduodenal ulcer. Roentgenologic examination of the stomach showed a round clear image in the antrum. Given a diagnosis of a gastric polyp, an operation was performed on this patient, and a tumor, the size of a hazelnut, was removed. Histological examination of the tumor showed aberrant pancreatic tissue in the gastric mucosa. The patient remained clinically and roentgenologically cured after the operation. The second patient had rapidly lost weight during the 3 months prior to consultation. A clinical, roentgenologic and endoscopic diagnosis of gastric cancer was made. A polyp, 10 cm. in diameter, was found during the operation and was surgically removed. Histopathological examination of the specimen showed an adenomatous polyp. Six months later the patient complained again of a gastric disorder and loss of weight. Roentgenologic examination of the stomach showed a tumor at the site which had been occupied by the first tumor. A gastrectomy with removal of the tumor was performed 1 year after the first operation. The tumor was the size of an orange. Histological examination showed gastric adenocarcinoma. The tumor originally removed had been kept in paraffin and was now histologically reviewed. Sections of the deep layers showed malignancy. The patient died 3 months after the second operation. The authors conclude that polypectomy is indicated only in cases of solitary, small, gastric, adenomatous polyps, no more than 1 cm. in diameter. Gastrectomy with ample removal of the polypous lesion is indicated in all cases of multiple polyps, regardless of their size, and also in cases of a solitary polyp, more than 1 cm. in diameter. The extension of the polypous lesions may in certain cases call for a total gastrectomy.

Sequelae of Total Gastrectomy and their Treatment. O. Rainer and S. Zollner. Arch. klin. Chir. **286**:539-553 (No. 6) 1958 (In German) [Berlin].

The authors report on 151 patients who underwent total gastrectomy at the district hospital in Klagenfurt, Austria, and on whom follow-up examinations were carried out in the last 7 years. Three forms of anemia were observed after gastrectomy: (1) anemia of iron deficiency; (2) abnormal com-

position of the blood of the pernicious anemic type; and (3) anemia of the aregenerative type. An early detection of the anemia of iron deficiency as well as of the masked sideropenia is important, since a cure will be obtained only by the administration of iron. When atrophic changes of the mucosa in the small intestine occur, intravenous treatment with iron becomes necessary. Duration of treatment depends on the iron deficiency as revealed by the capacity of absorption of iron, the normal level of which is about 200 mcg. per 100 cc. of blood. Anemia of iron deficiency with disturbances of absorption by the intestine requires intravenous administration of ferric saccharate. Emphasis is put on the fact that this administration of iron presents an unphysiological method, and consequently it requires control determinations of the capacity of iron absorption after 1,000 mg. of iron have been given. Disturbances of maturation of red blood cells, as evidenced by the presence of megaloblasts, can be prevented by the continued administration of vitamin B_{12}. Only one case of pernicious anemia was observed and that in a patient who discontinued the prophylactic treatment with vitamin B_{12} of his own accord. Reduced fat absorption necessitated greater fat intake at more frequent meals. The disturbed carbohydrate metabolism was examined in patients with the dumping syndrome. Results confirmed the necessity of restricting the carbohydrate, more especially the sugar, intake. A relationship between protein and iron metabolism was shown by the increase in beta globulin level in the serum of patients with iron deficiency. With a greater interval between the gastrectomy and the follow-up examination, the gamma globulin level in the serum increased.

Eosinophilic Granuloma of Bone. H. Hellner. Arch. klin. Chir. **286**:564-581 (No. 6) 1958 (In German) [Berlin].

Eosinophilic granuloma has been identified by this term since 1940, but the lesion was known before under several other names. Hellner presents 9 illustrating case histories. In the first 4 cases single foci existed; these were in the ilium in 1 patient, in the humerus in 2 patients, and in the femur in 1 patient. Single cranial foci existed in 3 patients, and the last 2 patients had multiple foci. The patients are usually young, about two-thirds being less than 20 years old. One or more lesions develop rapidly in some part of the skeleton, usually without noticeable symptoms. If the lesion is in the cranium, a bump may appear. Roentgenoscopy reveals a rapidly progressive osteolysis. The cranial lesions usually show no reactive marginal zone, but those in the diaphysis of the long bones are generally oval. The periosteal reactions accompanying the latter lesions often lead to erroneous diagnoses. Most frequently they are mistaken for osteomyelitis, but they have also been mistaken for sarcoma, myeloma, or myelosarcoma. Blood eosinophilia is not always present, but sometimes it is quite marked.

Single foci usually do not recur after surgical removal or roentgen-ray irradiation. Occasionally spontaneous cure takes place. Multiple foci, in the form of "eosinophilic granulomatosis" in young children, may develop into Letterer-Siwe's disease (xanthomatosis). Observations on patients with Hand-Schüller-Christian's disease (xanthomatosis of a cholesterol type) suggested that in some of these it was difficult to make a clinical differentiation from eosinophilic granuloma. The author believes, however, that in the classical form of Hand-Schüller-Christian's disease, with lacuna formation in the cranial vault, exophthalmos, and involvement of the pituitary, the differentiation from eosinophilic granuloma is clear. Today many observers are of the opinion that there are transitional lesions between eosinophilic granuloma and Hand-Schüller-Christian's disease. The author agrees with this on the basis of his own observations. From the clinical point of view it is most important for eosinophilic granuloma, particularly if it appears as a single lesion, to have a favorable prognosis, whereas the prognosis is unfavorable in Letterer-Siwe's disease and is doubtful (20% mortality) in Hand-Schüller-Christian's disease. It remains to be established whether the same causal factor, influenced by the age or reactivity of the patient, may produce these different forms of reticulosis.

Pitfalls and Success in Surgical Treatment of Focal Epilepsy. W. Penfield. Brit. M. J. **1**:669-672 (March 22) 1958 [London].

Commenting on the results of surgical therapy of focal epilepsy, Penfield says that the attacks were stopped in 41% of the cases, and the results were regarded as satisfactory in an additional 35%. The mortality has remained in the vicinity of 1.5% for a total of 470 patients. In this report the author is concerned with hazards and pitfalls that the neurosurgeon encounters in the surgery of atrophic epileptogenic lesions. Contrary to an earlier conception, simple adhesions between dura and arachnoid are not to be considered a cause of seizures unless the cortex has been lacerated, so that dural arteries enter the brain through the adhesions to anastomose with intracerebral arteries. If the surface of the brain is exposed for any length of time, it becomes injected, with the rapid appearance of small new vessels, and adhesions will form even if the surface is kept moist. The author believes that the pia becomes inflamed as the result of an exchange between brain and air that can occur through fluid but not through dura mater or membrane. The

injection of the pia disappears within a few minutes after pliofilm is laid upon it, provided that it has not been present too long.

Postoperative neuroparalytic edema is the second hazard discussed. It has been a habit to attribute the paralytic and irritative symptoms to edema of the brain. But it is probably more accurate to attribute both the symptoms and the edema to a common cause. The paralytic effect is usually most marked in the immediate vicinity of the cortical excision. Thus, one may expect transient loss of cortical sensibility in the arm after removal of parietal convolutions just posterior to the postcentral gyrus, and paralysis or paresis of the contralateral arm if the excision was located near the precentral gyrus. When the anterior portion of 1 temporal lobe is excised, there is usually transient weakness of the opposite side of the face. If the temporal excision is carried out on the dominant hemisphere, there may well be aphasia which develops about the second day and continues for 2 or 3 weeks. There may be an irritative effect as well as a paralytic one. The author has no idea what the cause of these local seizures may be. He calls them "neighborhood seizures" and expects them to occur perhaps once in 5 operations. They stop in a few days after there has been some increase in the administration of phenobarbitone.

Long-continued temperature elevation for a period of weeks means infection or aseptic meningitis. This latter condition is much more frequent after cortical excision of atrophic lesions in the treatment of focal seizures than it is after craniotomies for other purposes. The cause of aseptic meningitis seems to be the entrance into the subarachnoid spaces of a product derived from blood that has clotted in the wound. In order to prevent this reactive meningitis, it has been the author's practice to close the ventricle if it has been opened. This can be done with 2 or 3 sutures of silk placed in the ependyma, on either side of the opening, and tied loosely over a square of Gelfoam. When aseptic meningitis persists for more than 2 or 3 weeks, it may be wise to reopen the wound and close any fistula that may be present in dura or in ventricular wall. Commenting on the lesion left by excision, the author says that the operative wound does not often ripen into a new epileptogenic lesion. On the other hand, many partial failures must be due to the fact that not all the epileptogenic gray matter has been removed. Sometimes, of course, complete removal is not possible, owing to multiplicity of foci or because the function of the area to be removed is too precious. This is the surgeon's major dilemma. Adequate preoperative electroencephalographic study will keep him from operating on any patient whose focus of epileptic discharge lies in the brain stem. Incomplete removal can be detected by a second electrocorticogram, which may show increased activity of "spike" discharges in neighboring abnormal gyri. So the surgeon removes more of the lesions with the help of the electroencephalographer until at last he hears the welcome words, "All clear, no spikes."

Hemiplegia due to interference with lenticulostriate arteries is the most unsuspected pitfall of all. The author and his associate are preparing a special report on this problem. They believe that sudden paralysis may occur while gray matter is being removed from beneath the branching middle cerebral artery as it passes upward and outward over the insula and over the superior opercula. It seems most likely that some pulling or handling of the artery may cause occlusion of the perforating vessels that enter the perforated space which is situated just beyond. Although some of the 8 patients in whom the author observed this complication have recovered almost completely, he emphasizes that this is the most dangerous area for cortical removal.

Post-Traumatic Renal Insufficiency Without Oliguria. H. Smitskamp. Nederl. tijdschr. geneesk. **102**:215-220 (Feb. 1) 1958 (In Dutch) [Amsterdam].

Post-traumatic renal insufficiency can develop without an initial period of oliguria. The histories of 2 patients are presented whose urinary output increased to a minimum of 400 ml. in the first 24 hours after the trauma. The urea content of the blood, however, continued to rise, even after the output of urine had reached more than 1,500 ml. in 24 hours. The presence of extensive retroperitoneal and intramuscular hemorrhages, which added to the usual increase of post-traumatic protein catabolism, was regarded as an important contributory factor to the renal insufficiency. The infusion of hypertonic dextrose solution into the vena cava via a polythene catheter, together with rigid fluid control, resulted in rapid improvement and ultimate recovery.

Cutaneous Necrosis Due to Norepinephrine: Analysis of Reported Cases and Surgical Treatment. A. S. Close and W. H. Frackelton. Wisconsin M. J. **57**: 127-131 (March) 1958 [Madison].

Levarterenol (l-norepinephrine) is used in various hypotensive states, but its intravenous administration is often followed by ischemic complications. Close and Frackelton collected data on 55 instances of cutaneous necrosis resulting from the administration of levarterenol in 46 patients. The authors tabulate the data on many of these and on 6 of their own patients. To prevent extravasation, cannulas and catheters should be secured by ligatures. The muscular part of the arm should receive preference as the site of administration, because slough is more likely to occur in the lower extremity after prolonged administration, and where extravasation

is permitted. Two effective methods for preventing slough are presented: (1) the infiltration of ischemic areas with a saline solution of Regitine and hyaluronidase and (2) administration of levarterenol through a catheter in the iliac vein via a high saphenous phlebostomy.

Ischemic areas that will progress to necrosis have a typical appearance. They are cold, pale, and, if associated with localized extravasation, boggy. They are frequently tender. Since the majority of the patients who receive levarterenol are critically ill, it is wise to delay surgical treatment of the slough until the patient is out of danger. A thick, tough, black eschar usually forms in the area of necrosis and involves all layers of skin. The eschar remains impervious for 2 to 4 weeks, a period sufficient to permit enough improvement in the patient's general condition to warrant definitive treatment. The eschar is then removed at the bedside by sharp dissection. After several days of intermittent moist saline dressings, a thin split-thickness skin graft is removed and applied to the granulation bed with the patient under local anesthesia.

Experiences with the Surgical Treatment of Mitral Stenosis. J. A. Williams, D. Littmann and R. Warren. New England J. Med. **258**:623-630 (March 27) 1958 [Boston].

This report is based on a study of 52 patients (51 men and 1 woman) treated surgically for Mitral stenosis in a Veterans Administration hospital during the 5-year period ending in November, 1956. Since almost all the men had been able to pass physical examinations for military service in the not too remote past, it is probable, although not certain, that the valvular disorders in these cases were acquired relatively late in life or were of such minimal degrees as to escape detection. The 47 patients in whom the preoperative diagnosis of mitral stenosis was substantiated at operation are discussed first and are identified as group A. It is generally recognized that mitral disease is statistically less common in males than in females. Observation on these male patients suggested that the clinical patterns of mitral disease tend to be considerably less "typical" in males than in females. The unusual features in this predominantly male material were the frequency of hemoptysis before surgery (70%) and the prevalence of calcific involvement of the mitral-valve leaflets (83%). There were 6 operative deaths among the 47 patients on whom commissurotomy was performed; 3 were due to embolization, and 3 to cardiac failure. Follow-up studies indicated that 2 patients succumbed to recurrent rheumatic carditis and that, of the remaining 39 patients, 35 were benefited by commissurotomy. Improved functional status was usually, but not always, accompanied by reduction in pulmonary hypertension. No patient had recurrence of hemoptysis after surgery. Mention is made of a helpful electrocardiographic sign, the "T mitral," indicative of early hypertrophy of the right ventricle. This pattern consists of an unusually tall and sharp T wave after a wide P wave. It was evident in the tracings of 15 patients, all of whom had important degrees of mitral stenosis. The limitations of catheterization of the right side of the heart in the differential diagnosis of pulmonary hypertension are discussed.

The 5 patients in whom the diagnosis of mitral stenosis was incorrect are designated as group B. Three of these 5 were found to have preponderant mitral incompetence with little or no stenosis. Valvular calcifications, commonly regarded as indicative of mitral stenosis, had been detected fluoroscopically in 1 of these patients before surgery and were found in all 3 at operation. In the other 2 patients in this group, despite extensive studies including catheterization of the right side of the heart, a definite preoperative diagnosis could not be established. Hemoptysis had occurred in both; both were seriously disabled and had auscultatory signs of mitral stenosis. Exploratory cardiotomy revealed no disease of the mitral valve in 1 patient and questionable disease in the other. After operation, each patient continued his preoperative course of progressive disability until death, 18 months and 26 months respectively, after surgery. Autopsy performed on 1 of these patients established "idiopathic cardiomegaly" without anatomic valvular abnormalities or histological evidence of rheumatic heart disease. Although autopsy was not performed on the second patient, diffuse myocardial disease was considered on clinical grounds to be the primary cause of death.

Bacterial and Mycotic Endocarditis Following Cardiac Surgery: Report of a Case. B. H. Hyun, E. A. Dawson and R. E. Pence. J. Thoracic Surg. **35**:298-304 (March) 1958 [St. Louis].

The authors report on a 32-year-old man, with a preoperative diagnosis of predominant mitral insufficiency, in whom a total circumferential suture of the mitral ring was accomplished without apparent difficulty. The 5-finger annulus found on internal palpation of the mitral valve was reduced to a 3-finger diameter with favorable pressure changes. The insufficiencey was thought to be improved by 90%. After an uneventful immediate postoperative course, the patient's temperature rose to 104 F (40 C). Escherichia coli was recovered from the urine, and hemolytic Staphylococcus pyogenes var. aureus was recovered from the blood. A diagnosis of acute bacterial endocarditis was made, and penicillin was given by the intravenous route. For 8 days the temperature spiked between 99 F (37.1 C) and 104 F (40 C). From the 5th to the 8th week of hospitalization the temperature never rose above

98.6 F (37 C). Intravenous administration of penicillin was continued for 8 weeks, and then oral administration of penicillin was substituted. In less than 24 hours, chills and fever of 102 F (39 C) recurred. Intravenous administration of larger doses of penicillin was resumed, and at the end of the 9th week the patient's temperature was restored to normal and remained normal from the 10th to the 13th week when intravenous administration of penicillin was again discontinued and oral administration was started. Within 36 hours the patient's temperature once more began spiking and varied between 97 F (36.2 C) and 104.4 F (40.2 C) until death. Hemolytic Staph. pyogenes var. aureus was once more recovered from the blood during this period.

At autopsy a diffuse fibrinous pericarditis was found. A portion of the circumferential suture used to produce reduction in the size of the mitral annulus was found lying free in the left auriculoventricular lumen, having been misplaced at the time of the operation. Microscopically, the thrombotic material from the "purse string" contained colonies of staphylococci. In addition, this thrombotic material also showed extensive mycotic growth. The fungi, identified as Candida albicans, were arranged in a foliate pattern, showing septate myceliums and yeast-like cells. Fourteen cases of bacterial endocarditis after cardiac surgery were collected from the literature. Thus, while not a common complication, it occurs with sufficient frequency that it must be regarded as 1 of the hazards of such surgical intervention. In most of the cases hemolytic Staphylococcus organisms were the pathogenic agents.

Late Results of Direct Surgery of the Aortic Bifurcation and Its Major Branches. F. B. Cockett and A. G. Norman. Brit. M. J. 1:727-734 (March 29) 1958 [London].

A detailed follow-up study of 30 patients treated at St. Thomas's Hospital in London for either arteriosclerotic occlusion or aneurysm of the abdominal aorta and its major branches, who underwent direct arterial surgery during the last 5 years, is presented by the authors. Three different types of direct arterial surgery have been used: (1) replacement with stored homograft; (2) replacement with plastic prosthesis; and (3) endarterectomy or "rebore" of the occluded segment. Of 18 patients on whom replacement with stored homograft was performed, 2 died in the early postoperative period as a direct result of the operation, probably due to sepsis in the graft which resulted in late leakage and rupture of an anastomosis. Of the remaining 16 patients, there was a serious complication resulting in loss of a limb in 3 patients. Thirteen patients have had success in varying degree, and 10 of these obtained good results. As to the technique of inserting grafts, the end-to-side type of arterial anastomosis has proved superior over the end-to-end type. In fact, in the whole series there has not yet been a case of delayed occlusion of an end-to-side type of anastomosis. Of 6 patients on whom plastic prosthesis was performed, 2 had aortic thrombosis and 4 had an aneurysm of the aorta. One patient in each of these two groups died. The use of the polyvinyl sponge prosthesis was unsatisfactory in both patients with aortic thrombosis. Of the 4 patients with aneurysm, the 3 surviving patients obtained highly satisfactory results from replacement with Orlon tubes. The latter material may be preferred to the polyvinyl sponge. These findings suggest that in patients with arteriosclerotic thrombosis plastic material is unsatisfactory, while it is suitable in those who require a short-segment replacement of a large vessel such as the dilated aneurysmal aorta. The results were most encouraging in 6 patients on whom removal of an obstructing thrombus had been performed by way of "disobliteration" or "rebore." There were no deaths, there have been no major complications, and the follow-up results to date have been satisfactory. With improvements in the technique of "rebore," the authors believe that the indications for this type of operation can be considerably extended.

Coronary disease and cerebral thrombosis occurred in only 1 of the 20 patients who were under 60 years of age; only 4 (40%) of the 10 patients over 60 years of age had coronary disease. On the basis of these results surgical treatment is recommended for any patient in the under-60 age group with arterial occlusion. If the lesion is a localized occlusion with reasonably good artery on either side, direct removal of the occluding thrombus from the artery—"rebore"—is a sound and safe operation. If the arterial disease is more widespread, a better long-term result will be obtained by radical resection of the whole aortic bifurcation and bypassing the diseased segments on each side with a stored homograft. In the over-60 group one's attitude is tempered by the increased likelihood of other arteriosclerotic lesions such as angina. However, the benefits of this type of surgery far outweigh the risks.

The Surgical Therapy of Occlusive Coronary Artery Disease—Present Status. A. A. Bakst and L. Loewe. Am. J. Cardiol. 1:340-344 (March) 1958 [New York].

In an attempt to evaluate various surgical procedures designed to correct coronary artery disease by augmenting the extracoronary arterial collateral circulation, 2 physiological tests were performed on animals. The peripheral segment of the ligated circumflex coronary artery was cannulated, and a continuous flow of arterialized blood was obtained. This flow served as a measure of intercoronary collateral circulation. Next, perfusion experiments were

performed. With the heart of the animal in situ, the ascending aorta was clamped distal to the orifices of the coronary arteries. The descending aorta was cannulated, and the arch and the descending aorta were perfused with a neoprene latex solution at a pressure of 160 to 180 mm. Hg. Under these conditions, any material found within the coronary arteries could not have entered through their normal ostiums and must have arisen from extracoronary circulation.

The surgical procedures assessed in animals by these physiological tests were pericardial poudrage as described by Thompson, deepicardialization, i. e., a modification of pericardial poudrage as described by Harken and co-workers, and implantation of the internal mammary artery as described by Vineberg. Poudrage seemed effectively to fill the circumflex coronary artery in 50% of the animals. Implantation of the internal mammary artery showed good filling of the anterior part of the descending artery in 90% of the specimens and of the circumflex coronary arterial tree in 25%. It, therefore, seems that each of these procedures is effective in producing extracoronary collateral circulation to a segment of the coronary arterial tree. The authors' present concept has matured to a combination of pericardial poudrage and implantation of the internal mammary artery to protect both the anterior and the posterolateral portions of the left ventricle against coronary artery occlusion. This consists of the implantation of the internal mammary artery into the anterior wall of the left ventricle, combined with the instillation of magnesium silicate posteriorly and posterolaterally over the wall of the left ventricle. The modification of the Vineberg technique by performing it through an anterior approach not only facilitates the dissection of the vessel but also permits the patient to be placed in the supine position which is best tolerated by the cardiac.

Bronchography in Pulmonary Tuberculosis: Studies on Its Value in Patients Being Considered for Surgery. D. L. Merrill and P. C. Samson. Am. Rev. Tuberc. 77:561-592 (April) 1958 [New York].

One hundred thirty-one bronchograms were obtained from 105 patients who were admitted to the thoracic surgery service of the Highland-Alameda County Hospital in Oakland, Calif., during the year 1956. Of the 105 patients, 38 had proved tuberculosis and 5 were suspected of having tuberculosis. Repeat bronchograms were obtained from 10 of the 38 patients for observation of the course of the disease. Twenty-nine of the 38 patients had not received previous surgical treatment, and 9 had been operated on previously. The contrast medium used was Dionosil (3,5-diiodo-4-pyridone N-acetic acid); it proved to be useful because of its low viscosity, prompt absorption, and rapid excretion; it uniformly allowed visualization of the segmental bronchi and bronchioles, which was of considerable diagnostic value.

Bronchographic observations made in the 43 patients with proved or suspected tuberculosis and in those reported on by other workers seem to justify the following general conclusions. Bronchiectasis with terminal bronchostenosis of the segmental bronchus is usually the concurrent and early end-result of advanced parenchymal disease or of tuberculous endobronchitis. With such a bronchographic finding, the question of persistent disease and of the viability of "nonculturable" tubercle bacilli becomes much more acute; the incidence of recurrence may be considered sufficiently high to warrant resection. This holds equally true for "initial" as for "retreatment" patients. Bronchiectasis in patients with tuberculosis is evidence of previous or currently active disease in the segment involved. In the absence of terminal segmental stenosis, there is usually bronchiolar filling which indicates functioning lung with minimal disease. Whether these segments should be removed is questionable. The value of resecting or preserving such segments must be weighed according to the extent of other areas of involvement, the problems of postoperative space management, the susceptibility of the patient's tubercle bacilli to the available chemotherapeutic agents, and the patient's clinical course. At the present time the authors are not resecting additional segments on the bronchographic evidence of associated bronchiectasis alone.

Saccular bronchiectasis (either nonspecific or tuberculous), especially of the apical regions of the lung, is often the late result of chronic fibroid tuberculosis and may represent a source of infectious sputum or of recurrent hemoptysis, especially in older patients. Such lesions may require surgical treatment. The demonstration of cavities by direct filling with the bronchographic agent is sporadic and unreliable. Bronchography is of proved value in the diagnosis and evaluation of major bronchial disease associated with adjacent lymphadenopathy. Bronchography has considerable screening value in patients with recurrent or progressive clinical disease after previous surgical intervention. Unsuspected empyema spaces with bronchial communication (occult fistula) and the differentiation of such lesions from cavities involving the superior segment of the lower lobe or other areas are often possible with Dionosil. Bronchography has also proved useful in evaluating the effect of surgical intervention in selected cases, such as symptomatic bronchial torsion occurring after segmentectomy.

Bronchography is indicated before almost any surgical approach to the treatment of pulmonary tuberculosis. The preoperative delineation of anatomic and architectural anomalies, the finding of lobar, segmental, or subsegmental involvement

(especially in contracted areas of the lung), and the occasional observation of an unsuspected, but frequently significant, condition, such as a spontaneous bronchopleural fistula or nontuberculous basilar bronchiectasis, may be apparent with no other diagnostic technique. Bronchographic findings in patients with pulmonary tuberculosis are informative and of value in planning resective surgery, especially in patients with drug-resistant infections, in the management of residual lesions, and in the evaluation of residual disease after previous surgical intervention.

Vitallium Tube Method for Repair of Strictures of the Bile Ducts. D. W. McGoon and O. T. Clagett. Surg. Gynec. & Obst. **106**:409-412 (April) 1958 [Chicago].

The authors describe experience with the Vitallium tube method of repair of the biliary ducts at the Mayo Clinic since its first application in 1944. All 52 patients who have had a Vitallium tube inserted into the biliary ducts during the repair of strictures of those ducts and reestablishment of end-to-end continuity are included in this study. Adequate follow-up information to October, 1956, was available on all but 4 of the 52 patients. Previous operations on the biliary tract appeared to mark the onset of the stenosis in every instance except 1, and it is assumed that injury to the ducts at operation caused the stenosis. The 1 exception was a 16-year-old boy who sustained injury to the biliary ducts from a bullet that penetrated this region. The operation in which the Vitallium tube was inserted occurred from 2 months to 13 years after the surgical procedure that appeared to have caused the stricture, but most commonly 6 to 18 months had elapsed.

Originally, it was hoped that the Vitallium tube, situated within the biliary duct at the site of the stricture, would remain in place and continue to function indefinitely. A number of these patients returned with recurrent biliary obstruction, and removal of their heavily encrusted and occluded Vitallium tubes became necessary. The operation for the insertion of the Vitallium tube resulted in 1 death; this patient was a very ill women who had had 4 previous attempts at surgical correction of her stricture during the preceding 6 years. She died in a hepatic coma 10 days after the operation. One other patient died of "nephritis and uremia" 9 days after removal of the Vitallium tube elsewhere. The results in 7 of the 48 patients are classified as indeterminate. In 2 of these, removal of the Vitallium tube occurred less than 1 year ago, and although these patients have been doing well thus far, the final result cannot yet be safely estimated. The surgical treatment of the other 5 patients deviated from the scheme outlined in that additional and probably unnecessary procedures were performed at the time of removal of the Vitallium tubes, thus obscuring the final result of the operation as it is now conceived.

The Vitallium tubes have never been removed from 15 patients. Two of these patients have died of causes unrelated to their hepatic and biliary systems. The shortest interval since insertion of these tubes is 14 months. Seven patients still have their Vitallium tubes in place and functioning satisfactorily 11 or more years after insertion. Twelve patients have remained well after removal of the Vitallium tubes. The remaining 14 patients must be regarded as representing failures of the method if critically studied, although 3 of these patients have had a satisfactory result after a second trial of the Vitallium tube method of repair. Only after exploration of the region of the biliary ducts is a decision for or against employment of the Vitallium tube method made. The authors feel that the Vitallium tube is a highly effective method of treating patients with biliary strictures in whom there is no upper remnant of duct extending beyond the scarred undersurface of the liver.

Peripheral Arterial Emboli. W. C. McGarity, W. D. Logan Jr. and F. W. Cooper Jr. Surg. Gynec. & Obst. **106**:399-408 (April) 1958 [Chicago].

The authors review observations on 64 patients who had a total of 86 peripheral arterial emboli. These patients were treated at 3 hospitals during the 10-year period from 1946 to 1956. There were 40 males and 24 females. The youngest patient was 13 years old, and the oldest was 87. All but 13 patients were between 40 and 80 years of age, and the peak incidence was in patients between 50 and 70. The authors also review the literature analyzing 2,088 cases and 1,167 embolectomies. Mural thrombi formed on the left side of the heart account for most of the peripheral arterial emboli. Rheumatic heart disease and heart disease after myocardial infarction are the most common causes. A mural thrombus forms within the lumen of the left side of the heart during arrhythmia or after injury to the heart wall and then dislodges to settle elsewhere. Frequently, the patient's history shows that changes have been made recently in his medical treatment or that there has been an alteration in his pulse rate or heart rhythm.

More than 40% of the 86 emboli in the authors' series occurred in the femoral vessel. Vessels of the upper extremities accounted for 18.6%. These percentages are in close agreement with those derived from a review of 2,088 peripheral arterial emboli reported in the literature. Any embolus may be 1 of a series or 1 of several occurring simultaneously. Sixteen of the 64 patients had more than 1 embolus. Auricular fibrillation and myocardial infarction were responsible for the majority of these multiple emboli. Pain or paresthesia at the site of the lesion

or distal to it constitutes the most frequent initial symptom of arterial embolus. Treatment of arterial embolus is a medical emergency. The ultimate outcome depends largely upon early recognition and treatment. Not every patient with an arterial embolus is a candidate for embolectomy. Conservative treatment is indicated (1) for patients so critically ill from other diseases or from simultaneous cerebral or visceral embolism that any but supportive treatment may be hazardous and (2) for patients with adequate collateral circulation in the affected extremity. In these patients, sympathetic blocks should be administered immediately to relieve the reflex spasm of the collateral vessels.

In the 64 patients the most frequent site of occurrence was at the bifurcation of the common femoral artery. The best results were obtained when treatment was started within the first 6 to 12 hours after occurrence of the embolus. Seventy per cent of the embolectomies in the series presented by the authors were successful as compared with 38% of the 1,167 embolectomies for which results were given in the reviewed literature. The mortality rate in the 64 patients was 29.6% (12 or 18.7% in the surgically treated group and 7 or 10.9% in the conservatively treated group). Most of the deaths were due to associated diseases. When an embolus lodges in the popliteal vessel or in an artery of the upper extremity, the choice of treatment should be based on the specific findings in each case. When an embolus involves the aorta or the iliac or femoral arteries, it should be treated as a surgical emergency, provided that the patient's condition will permit.

Experience with Triethylene Melamine (TEM) and Triethylene Thiophosphoramide (ThioTEPA) in Recurrent or Metastatic Solid Tumors. R. F. Schell. Surg. Gynec. & Obst. **106**:459-465 (April) 1957 [Chicago].

The authors report their experience with triethylene melamine (TEM) and triethylene thiophosphoramide (ThioTEPA, TSPA) in 40 patients with advanced, "hopeless" cases of carcinoma in whom all curative and all established palliative measures had failed or were contraindicated. The purpose of instituting treatment in these advanced cases was twofold: (1) to determine whether these agents significantly inhibited tumor growth and (2) to attempt to make the patient's final remaining days as comfortable as possible. The treatments did not ordinarily impose a severe burden on the patient's financial or physiological economy, and in many cases gave a great psychological "lift" by offering some relief to an intolerable situation. ThioTEPA was given as an injection of a solution containing 10 to 20 mg. per cubic centimeter either intramuscularly for general effect, or into serous cavities to attempt to control malignant effusions, or directly into tumor masses. TEM may also be utilized in a variety of ways and has the advantage of being effective when given by mouth. In this series it was utilized most frequently by being instilled into a serous cavity in a dosage of 5 to 10 mg. Subsequent therapy consisted of the oral administration of the drug in divided doses of 2 to 5 mg. a week, given with bicarbonate of soda one-half to 1 hour before breakfast to lessen gastric irritation and to promote absorption. Occasionally TEM was given by intramuscular injection or by direct injection into tumor masses.

A clinical response was obtained in several cases of adenocarcinoma, particularly those primary in the breast, by systemic therapy with ThioTEPA or the injection of this agent directly into tumor masses. TEM appears to be preferable to ThioTEPA in the control of malignant effusions. No effect from either of these agents was seen in squamous-cell tumors or in mesenchymal tumors arising in organs other than the lymphatic system. The depressant effect of these agents on the bone marrow was the chief cause of complications. In selected cases the use of the antitumor compounds, TEM and ThioTEPA, has been of assistance in easing the distress of terminal cancer cases. It has occurred to several workers in this field that the prophylactic administration of carcinocidal agents at the time of surgery to render the soil less fertile for the implantation of cancer cells could well be helpful. This procedure was started by the author on a limited scale with the use of a single intramuscular or intravenous dose of ThioTEPA immediately after surgery for carcinoma of the breast, and the intraperitoneal administration of TEM after extirpative surgery for abdominal cancers.

A Ten Year Study on Wound Infections. P. Dineen and C. Pearce. Surg. Gynec. & Obst. **106**:453-458 (April) 1958 [Chicago].

The records of the New York Hospital-Cornell Medical Center were studied to find patients with wound infections, occurring between Jan. 1, 1947, and Dec. 31, 1956, on the general surgical service and surgical specialties. There was a total of 511 wound infections during this period. These form the basis of this study. Wound cultures were inoculated for primary isolation both aerobically on blood agar plates and in 3% beef infusion broth, and anaerobically in liver dextrose broth. Recently, since the establishment of the surgical bacteriology laboratory, staphylococci have been characterized by mannitol fermentation, coagulase production, antimicrobial susceptibility profile, and phage typing as well as by the production of hemolysin and pigment. Drug sensitivity tests were not done except by the disk method, and in the earlier years of this study these were carried out only upon

request. Analyses were made of yearly and monthly incidence, surgical service involved, and species of organisms involved. The rate of infections varied from 0.8 to 1.4% with an over-all rate of 1%.

Infections that occur in the postoperative state are in the great majority of instances caused either by staphylococci or by one or more of the enteric flora. The incidence of wounds infected with intestinal flora has not appreciably changed in the past 10 years, and the seasonal curve does not indicate any significant variation. Because more wounds are infected with staphylococci and in view of the current intense interest in this problem, the present survey was made. Fluctuations in the annual number of infections are comprised almost exclusively of staphylococcic infections. Peak months for staphylococcic wounds in this center are March and December. These peak months of wound infections coincide with the peak months of upper respiratory tract infections. Nasal cultures from 5 surgeons doing most of the major surgery showed them to have coagulase-positive, penicillin-resistant Staph. aureus present during March and April of 1957. In March there were 10 staphylococcic wound infections and in April none. Therefore, it is apparent that the mere carrying of staphylococci does not cause wound infection. Wound infections are usually caused by breaks in technique, a weakened host resistance, or by "persistent" organisms. Increased vigilance on the part of the professional staff is probably the single most important factor in prophylaxis. Attention should also be directed to adequate face masks, to operating-room ventilation, and to the prevention of the "carrier state" by the patient and the professional staff.

NEUROLOGY & PSYCHIATRY

Neurosis Tarda and Heart Infarct. F. J. Tolsma. Nederl. tijdschr. geneesk. **102**:322-325 (Feb. 15) 1958 (In Dutch) [Amsterdam].

The author employs the term "neurosis tarda" when a neurotic syndrome appears in a patient over 40 years of age. He observed 8 patients in whom this was the case after an unrecognized heart infarct. The history of these patients gave no indication of a hereditary tendency or of clinical symptoms of a neurosis. The case records of 5 of these patients are given. They complained of being easily fatigued and showed signs of nervousness and anxiety. Electrocardiographic examination revealed in all the signs of an old heart infarct. It is also noteworthy that none of these patients showed signs indicating the existence of arteriosclerosis. There was a change in character accompanied by psychoneurotic manifestations which took the form of anxiety neurosis, neurasthenia, or hysteriform symptoms. Explaining to the patient that he has had a mild heart attack and suitable psychotherapy are the most important therapeutic measures. Some restriction in physical activity may also be necessary; this will depend on the physical as well as on the psychological status of the patient.

New Method of Phenobarbitone Administration in the Treatment of Epilepsy. D. C. J. O'Connor. Lancet **1**:609-611 (March 22) 1958 [London].

O'Connor believes that changing blood levels of phenobarbital explain why preparations of phenobarbital now in common use are not completely successful, toxic effects being caused when the level is high and fits appearing when it is low. He tried a preparation which releases phenobarbital slowly over a long period and which might be expected to produce a more constant blood level. He reports results in epileptic patients in whose treatment phenobarbital "spansules" were substituted for the same drug taken in the form of tablets or solution. Each spansule contained 1½ grains (0.1 Gm.) of phenobarbital in coated granules, which released the drug at a uniform rate, ensuring a steady absorption over a long period. The 18 psychotic, epileptic patients in whom phenobarbital spansules were used had had convulsions and psychoses for more than 10 years. They were examined every 4 months as inpatients and were followed up throughout 1955, 1956, and 1957. The same nurses attended the patients, and the same scheme of interpreting and recording convulsions was followed over the 3 years. The epilepsy was classified as dementia paralytica with major and minor convulsions in 1 patient, post-traumatic Jacksonian epilepsy in 1, idiopathic petit mal in 2, post-traumatic grand mal in 1, and idiopathic grand mal in 13, with hysterical overlay in 1 and periods of status epilepticus in 1.

These patients had the severest form of epilepsy, both in the psychosis and in the frequency and severity of convulsions. The patients were investigated by means of frequent blood and urine studies, chest and skull roentgenograms, and complete physical and neurological examination, with particular attention to tests of speech, walking, and muscular coordination and balance. Before the changeover, the mean daily dose of phenobarbital in the 13 patients receiving it was 2.8 grains (0.18 Gm.); with spansules the mean daily dose in the 18 patients was 5.8 grains (0.37 Gm.). In a few of the patients with severe epilepsy, up to 5 spansules (7½ grains [0.5 Gm.]) were given daily with no ill-effects. The reduction in the number of convulsions, both major and minor, was gradual and progressive after the changeover to phenobarbital spansules. In the 6 months before their introduction the group of 18 epileptic patients had a total of 385 convulsions; in the last 6 months of treatment with spansules the total was 7. The personality and mental state improved in most cases, and toxicity

was much reduced. The good effects and low toxicity are attributed to the constancy of the blood barbiturate level that was attained.

Treatment of Homosexuality by Individual and Group Psychotherapy. S. B. Hadden. Am. J. Psychiat. 114:810-815 (March) 1958 [Baltimore].

The author reports a few impressions gained from the individual treatment of homosexuals over almost 30 years, from their treatment in groups with other neurotics, and from their progress in groups made up exclusively of homosexuals. In selecting these patients, only males were included who have persistently and consistently in adult life preferred sexual experiences with those of the same sex and who have had some degree of rejection or revulsion toward sexual union with females. When 3 such patients were forced into private treatment almost at the same time, an opportunity presented itself to initiate a psychotherapy group made up exclusively of active homosexuals. After several preliminary individual sessions, the group was started. Two of the members were 22 years old; the third was 19 years old. The 2 older patients had been active homosexually for over 5 years; the youngest member had had an active homosexual career from the age of 12. At the first session the author learned that all 3 patients were casually acquainted and had often seen each other in homosexual haunts. Their feelings about homosexuality were initially explored. As consideration of their activities progressed, the front-page story of the murder and dismemberment of a sailor by a homosexual known to all 3 of them was discussed. The group sought an explanation of why homosexuals committed such violent crimes, and when it was suggested that only they could supply the answers after examination of their own feelings, anxiety mounted as they disclosed violent emotions activated by threats of exposure and blackmail. Before the first session ended, they were in agreement that homosexuals were not as gentle and artistic as they appeared. At this and several subsequent group meetings not only were murders among homosexuals discussed but their frequent suicides as well. The group's various fantasies in relation to homosexuality were explored, as were the unsatisfactory parental relationships, the disturbed nature of identification with their own sex, and the factors which led to arrest of their psychosexual development. At no time in this and in a second exclusively male homosexual group of 7 members was any attention focused on the nature of their homosexual experiences or the frequency of indulgence. The lack of prying on the part of the therapist is necessary to provide a beneficial experience to all patients.

In such groups the rationalization that homosexualty is a pattern of life the patients wish to follow is destroyed by their fellow homosexuals. This breaking down of their rationalization activates anxiety, and a desire to change is created. Obvious ego-strength is gained by identification with others who are also seeking socially acceptable goals. Identification with a group that has a healthy motivation soon banishes the feelings of isolation from which they suffer. When members reach the point where their homosexual drives have diminished or disappeared and they must completely reject all homosexual identifications and identify with heterosexuality, they are aided in final commitment by fellow members. This result is in contrast to patients in individual treatment, who may discontinue because they cannot make the final commitment; they develop anxiety about the loneliness which may result from giving up their homosexual connections and reach a critical point at which there is likelihood of regression. The group treatment convinces its members that their homosexuality is not an affliction or trick of fate but a pattern of inadequate behavior which can be changed.

Vaccination Against Poliomyelitis: Its Present and Future Status. L. L. Coriell. A. M. A. J. Dis. Child. 95:349-358 (April) 1958 [Chicago].

Three years of increasingly widespread use of killed poliomyelitis vaccine have coincided with marked reduction in reported cases of poliomyelitis. A particularly low incidence and a low-paralytic rate are the otustanding features of the 1957 season. Up to Nov. 15, there had been 1,988 cases of paralytic poliomyelitis reported for 1957, compared with 6,196 for the same period in 1956 and 9,796 for 1955. The decrease in 1957 occurred in all age groups, with a relatively greater proportion of cases occurring in patients from birth to 4 years of age. Estimates suggest that protection against paralytic disease approached 90% in patients who had received 3 or more properly spaced injections of vaccine. About 28 million of the 109 million persons aged less than 40 years have received a full course of 3 injections of vaccine. At least 17 strains of Coxsackie or enteric cytopathogenic human orphan (ECHO) viruses can cause a clinical disease resembling nonparalytic or occasionally paralytic poliomyelitis. These infections have almost certainly been called poliomyelitis in the past. Further research will show how many of the vaccine failures are infections caused by one of these other viruses.

The vaccine is safe, at the sacrifice of some potency. Suggestions for further research to improve potency are (1) disproportionate mixing of the 3 virus fluids in making the vaccine, (2) increasing the potency requirements, and (3) selection of new strains of virus. Such changes take time, and a more potent vaccine will probably not be available before the next poliomyelitis season. In the meantime, one must use the vaccine which is at hand, and the immediate objective should be to com-

plete 3 properly spaced infections for all persons less than 40 years of age. The use of vaccine during 2 epidemics in 1955 and 1956 did not show any beneficial effect on the course of the epidemic. This emphasizes the importance of doing vaccination ahead of time, and all physicians are urged to cooperate by completing immunizations.

On the basis of the data now available, a 4th injection of vaccine is indicated in the spring of 1958, just before the next poliomyelitis season. This is based on the following observations: 1. Although the vaccine is safe and effective, some paralytic cases continue to occur in triple-vaccinated children. 2. Protection appears to be proportioned to the amount of antigen injected. 3. Many children have received incomplete series, improperly spaced injections, or vaccine of poor potency. 4. There seem to be remarkably few reactions or contraindications to the vaccine. This proposed 4th injection is viewed not as a booster but rather as a method for completion of the primary immunization of those who for one reason or another failed to develop an immunological response to previous injections. The actual need for booster shots after this primary immunological response has not been demonstrated and may not be necessary at all after the population is once immunized, except perhaps in infancy and early childhood. At any rate, decision on a permanent plan for future booster shots should certainly be deferred pending more research.

GYNECOLOGY & OBSTETRICS

Treatment of Vaginitis Due to Trichomonas Vaginalis with 2-Acetylamino-5-Nitrothiazole. P. E. Bertoli. Minerva ginec. 9:1006-1010 (Dec. 31) 1957 (In Italian) [Turin, Italy].

Topical therapy of vaginitis due to Trichomonas vaginalis affords only a temporary remission of symptoms, which is followed by endogenous reinfection. The author administered an Italian proprietary preparation, Tritheon (2-acetylamino-5-nitrothiazole-Trichoman), to 2 groups of patients with this form of vaginitis. The first group was treated orally, and the second with a combined topical and oral administration of the drug. The first group, consisting of 23 women, received Tritheon in daily dosage of 300 mg. for 8 days. The patients were reexamined for the presence of T. vaginalis 3 times after the discontinuance of therapy. At the first examination 13 women (56%) had no clinical symptoms of the disease. The second course of treatment brought about complete remission of symptoms in 6 of the remaining 10 women (60%) who had still been positive for the protozoan at the first post-treatment examination. In addition, specimens of spermatic fluid were obtained from 11 husbands of the patients. Six of them, who were infected with T. vaginalis, received Tritheon in daily dosage of 300 mg. for 20 days. The therapy was effective in 5 men.

Better results were obtained with the combined therapy which was given to 25 women in the second group. These patients received Tritheon in daily dosage of 800 mg. divided into 300 mg. given orally and 500 mg. given topically. The first course of treatment brought about complete remission of symptoms in 18 patients (72%). The second course of treatment resulted in complete remission of symptoms in 5 of the remaining 7 patients (71%) who were still infected at the end of the first course. The drug was well tolerated and the author recommends its prolonged use in the management of vaginitis due to T. vaginalis.

Ovarian Function After Combined Surgical and Radiologic Treatment of Early Cervical Cancer. C. Krebs and N. Blixenkrone-Møller. Acta radiol. 49:128-136 (Feb.) 1958 (In English) [Stockholm].

In 18 women, between the ages of 22 and 37 years, with cancer of the uterine cervix, who were given irradiation treatment, an attempt was made to protect the ovaries against the irradiation effect by moving them, before irradiation, from their normal site in the small pelvis and fixing them as far away from the irradiated field as possible without impairing the blood supply. Nine of the 18 patients had cancer of the uterine cervix in stage 1, 6 had cancer of the uterine cervix in stage 2, and 3 had cervical cancer in stage 3. An inferior midline laparatomy was performed. The ligament of the ovary was divided and the ovary with the infundibulopelvic ligament mobilized, care being taken that the blood vessels of the ovary were left intact. The ovary was then lifted up and fixed with silk-knot sutures to the margins of a small incision into the parietal peritoneum on the psoas muscle or retroperitoneally to this muscle, so that the ovary occupied a position above the linea terminalis of the pelvis. The distance between the cancer of the vaginal portion of the uterine cervix and the lower pole of the ovary was usually 13 to 15 cm., and in a few patients up to 18 cm. The oviduct was removed only in exceptional cases, generally if it presented signs of chronic inflammation. Unilateral lifting of the ovary was performed in 7 patients, and bilateral lifting was done in the remaining 11. Five to 8 days after the operation, radium therapy or combined radium-and-roentgen therapy was instituted. The beam of roentgen rays was, as far as possible, directed downwards, away from the new site of the ovaries.

The 18 patients were followed for 6 to 7 years. Of the 9 patients with cancer of the uterine cervix in stage 1, 8 were alive without signs of recurrence after 6½ years and 1 died of recurrent cancer 12 months after the treatment; of the 6 patients with

stage 2 cancer, 4 were alive and well without any signs of recurrence; and 1 of the 3 patients with stage 3 cancer was alive and well after 6½ years. Of the 13 surviving patients, 8 had received radium therapy alone and 5 had received combined radium-and-roentgen therapy. Menstrual function was preserved in 6 of the 8 patients who had been given radium therapy alone. Six years after the treatment 1 of the 6 patients became pregnant but had an abortion at the 4th month. Menstrual function was not preserved in any of the 5 patients who had received combined irradiation therapy. These data suggest that neither the lifting of the ovaries nor the preserved ovarian function has aggravated the prognosis of patients with cancer of the uterine cervix, and that it is possible to avoid premature menopause induced by the irradiation therapy in most of the young women with early cervical cancer who can be treated with radium alone.

Pregnancy After Pneumonectomy on Account of Pulmonary Tuberculosis. C. D. Laros. Nederl. tijdschr. geneesk. **102**:264-268 (Feb. 8) 1958 (In Dutch) [Amsterdam].

The author attempted to obtain information regarding the course of pregnancy in women who had undergone pneumonectomy for pulmonary tuberculosis. He was able to collect information on 64 women who had had a total of 74 pregnancies after this operation. Seventy of the pregnancies resulted in the birth of healthy children. Three of the 4 stillbirths occurred in the same woman. A connection with the maternal tuberculosis was established in none of the 4 stillbirths. In general, no adverse effect of the pneumonectomy was observed during pregnancy or labor.

PEDIATRICS

Progression of Amaurotic Family Idiocy as Reflected by Serum and Cerebrospinal Fluid Changes. S. M. Aronson, A. Saifer, A. Kanof and B. W. Volk. Am. J. Med. **24**:390-401 (March) 1958 [New York].

The authors performed serial biochemical studies on 19 consecutive patients with amaurotic family idiocy, 1 patient with lipid histiocytosis of phosphatide type (Niemann-Pick disease), and 1 patient with diffuse sclerosis. There were 8 boys and 11 girls with amaurotic family idiocy, and their ages at the onset of the disease ranged from 4 to 9 months. Twelve of the children died, and autopsy was performed on 10. The clinical diagnosis in the 19 patients was based on the collective presence of apathy, progressing weakness, amaurosis, arrested development, emergency of abnormal movements, hypersensitivity to sound, and macular degeneration. The children were all of Jewish extraction. The patient with Niemann-Pick disease, a boy aged 5 months at the onset of the disease, and the patient with diffuse sclerosis, a girl aged 6 years and 3 months, are alive. An attempt was made to equate certain consistent changes in the serum and the cerebrospinal fluid with the clinical and the pathological course of the 3 disorders in the 21 patients.

The serum aldolase level, initially normal in the early phase of amaurotic family idiocy, became significantly elevated after about 9 months of clinically evident illness, coincident with the emergence of skeletal muscle atrophy. The latter was believed to be caused by the observed acceleration of lower motor neuron breakdown. In the protracted phase of amaurotic family idiocy, the serum aldolase level generally regressed to normal values. A roughly similar pattern was observed in the patient with Niemann-Pick disease, which is a disorder presenting a central nervous system anatomic component almost identical with amaurotic family idiocy. No comparable changes in serum aldolase level were seen in the patient with diffuse sclerosis or other long tract or upper motor neuron diseases studied.

The serum glutamic-oxalacetic transaminase level was consistently and markedly elevated during the entire course of the disease in all patients with amaurotic family idiocy and in the patient with Niemann-Pick disease. The hypertransaminasemia tended to lessen during the protracted phase of these disorders. In contrast, the girl with diffuse sclerosis (and patients with other neurological disorders) showed normal or minimally elevated values. High transaminase levels were also noted in the cerebrospinal fluid of the patients with amaurotic family idiocy and Niemann-Pick disease. The cerebrospinal fluid transaminase level was depressed in the patient with diffuse sclerosis. These data indicate that the extensive and continuing ganglionic disintegration of amaurotic family idiocy is sensitively mirrored by elevated transaminase levels in the serum and in the cerebrospinal fluid.

The level of total serum neuraminic acid was nonspecifically elevated in the 3 neurological disorders principally studied, in contradistinction to the singular elevation of this substance in the cerebral tissues in amaurotic family idiocy. However, the serum protein-linkage distribution of this substance in these 3 diseases showed a distinctly abnormal pattern, as indicated by the ratios formed by globulin neuraminic acid/total neuraminic acid and globulin neuraminic acid/globulin protein. A significant depression of serum and cerebrospinal gamma globulin levels also was observed in the patients with amaurotic family idiocy. The evidence presented seems to indicate the possibility that the pathophysiological substrate of amaurotic family idiocy may extend beyond the confines of ganglionic degeneration.

Relapses of Tuberculous Meningitis in Children. V. N. Kritsky. Pediatriya 36:34-40 (Jan.) 1958 (In Russian) [Moscow].

One hundred four children who had had tuberculous meningitis were under observation at the Children's Tuberculous Sanatorium of the Voronezh Region. Eighteen (9.5%) children had relapses. They were treated with streptomycin (subarachnoidally and intramuscularly) and after 1951 with streptomycin coupled with PAS and phtivazid. Relapses of tuberculous meningitis were more common in children with hematogenic manifestations of tuberculosis, as well as in those with delayed treatment. Most frequently they occurred in the first 12 months from the onset of the disease. These manifestations were provoked by infections, overcooling, trauma, etc. During the last years relapses were fewer in number due to advanced methods of treatment and early diagnosis.

Spontaneous Perforation of Biliary Passages in Infants. R. Funder. Tidsskr. norske lægefor. 78:184-185 (March 1) 1958 (In Norwegian) [Oslo].

Spontaneous perforation of the biliary passages in infants is a rare condition but one it is important to know because immediate surgical treatment is necessary. Some weeks after birth, in an infant previously perfectly well, more or less acute onset of the following symptoms occurs: increasing apathy with crying, vomiting and meteorism, slight jaundice of intermittent type, light stools, dark urine, and slight fever. In the case reported in an infant aged 2 months, laparotomy with injection of indigo carmine via the gallbladder revealed a small perforation in the anterior wall of the hepatic duct at its junction with the cystic duct. A polyethylene tube was placed in the choledochus duct, and the perforation was closed over the tube. The postoperative course was uneventful. Three months after discharge the child was well. The importance of preoperative cholangiography is stressed.

Murmurs in Children: A Clinical and Graphic Study in 500 Children of School Age. A. A. Luisada, O. M. Haring, C. Aravanis and others. Ann. Int. Med. 48:597-615 (March) 1958 [Lancaster, Pa.].

A clinical and graphic study of systolic murmurs was made in 470 unselected children, between the ages of 4 and 14 years, and in 30 adolescents, between the ages of 15 and 17 years. There were 245 boys and 255 girls. Of the 500 children, 350 were white, 146 were Negro, and 4 were Indo-American. Clinical auscultation was made by 3 examiners. Electrocardiograms and phonocardiograms were obtained from all children. Additional clinical and graphic studies were made in 87 children with louder murmurs. Fluoroscopy was done in 40. Hematological studies were made in 38. From a clinical point of view, a medium or loud systolic murmur was detected in 23.3%, and no significant difference was found between the 2 sexes. Even though most of the systolic murmurs were pulmonic, a fair number were heard at the apex and over the aortic area. No correlation was found between murmurs and economic background or race. No correlation was found between murmurs and height or weight. Changes of the murmur with changes of position of the child or by rotating the neck were found to be inconstant and not relevant. No prolongation of the QT interval was found in children with murmurs. A phonocardiographic study revealed diastolic extra sounds in 63% of the children studied and a split pulmonic sound in over 50%. A study of the configuration of the murmur and of the area in which it was best recorded was made. With faint murmurs excluded, 23% of the children had murmurs in the tracing. The murmur was "musical" in more than 50% of the children; it was "diamond-shaped" in slightly less than 50%; and it was "in decrescendo" in more than 50%. This study would seem to indicate a mitral origin in over 50% and a pulmonic or aortic origin in the remainder. In 6.5% of the children, significant differences were found between the results of clinical examination and phonocardiographic findings. Regarding anemia, no difference was found between children with murmurs and those without. Fluoroscopy revealed a dilated and strongly pulsating pulmonary artery in 75% of children with louder murmurs.

The following possibilities were considered and excluded: (1) that the murmur is inherent in the size and configuration of the cardiovascular system of the child; (2) that it is caused by a disproportion in the development of heart, vessels, and ostiums; (3) that it is due to compression of the pulmonary artery by the chest wall; and (4) that it is an extracardiac murmur or is due to anemia or is originating in the neck. It was also excluded that the systolic murmurs of children have different clinical or graphic characteristics from those of "organic" murmurs. The frequency of occurrence of apical and aortic systolic murmurs was not considered as implying a "physiological" origin. Many diseases in man, such as coronary arteriosclerosis, dental caries, or baldness, the incidence of which is extremely common, are not considered physiological. In an attempt to ascertain whether an extremely discrete form of rheumatic fever may provide an explanation for the systolic murmurs of children and adolescents, postmortem examinations were performed on 500 unselected persons over 5 years of age. These studies revealed the extreme frequency with which the cardiac valves present minor damage. This frequency increases with age; lesions were found in 20% between the ages of 11 and 15 years. The coincidence of this figure with that of medium or loud murmurs observed by the

authors is striking. These minor valvular lesions were considered by pathologists as being of rheumatic nature. However, further proof of this may be needed. Two alternative concepts are presented: (1) that the murmurs are caused by a discrete rheumatic process which has different characteristics from the more severe forms and which, in most cases, is not followed by important valvular lesions and (2) that the murmurs are due to nonrheumatic, possibly allergic valvulitis, with no tendency to increase in severity. In either case, it is to be considered impossible to separate these murmurs from those of valvular lesions which have greater clinical significance. Therefore, the authors advise careful notation of all murmurs and repeated studies through the years. Mitral stenosis would never be accidentally discovered in patients between the ages of 20 and 40 years if careful, systematic studies of children were made and observations were continued until a murmur either disappeared or became definitely significant.

DERMATOLOGY

Lepromatous Leprosy: Combined Treatment with Sulfone, Streptomycin and Isonicotinic Acid Hydrazide. O. Orsini. Arq. mineir. leprol. **17**:291-294 (July) 1957 (In Portuguese) [Belo Horizonte, Brazil].

According to the literature, the administration of sulfones alone in the treatment of persons with leprosy favors the development of pulmonary tuberculosis or aggravates the lesions of pulmonary tuberculosis. A combined treatment with sulfones, streptomycin, dihydrostreptomycin, and isonicotinic acid hydrazide causes a marked regression of both the pulmonary and the leprotic lesions. It often produces complete recovery from both diseases.

A married woman, 40 years old and the mother of 2 children, requested treatment for what she thought were leprotic lesions. The patient had had contact for 6 years with a servant who had lepromatous leprosy. Contact was lost when she learned that the servant had the disease. Ten years later hypochromic spots appeared on the legs of the patient. In the course of 3 years the spots became dark in color. Erythematous lesions appeared on the face. Small nodules appeared on the arms and legs. There was a complete tactile anesthesia of the feet. The results of the Wassermann and Mitsuda reactions were constantly negative. Tests for Mycobacterium leprae in the nasal mucus and in exudates of the nodular lesions became positive after a few years of having been negative. The patient used irregularly for more than 1 year a sulfone preparation in tablets taken by mouth. Then she complained about respiratory symptoms and moderate fever. Roentgenologic examination of the chest showed early lesions of bilateral pulmonary tuberculosis. Treatment consisted of the administration of sulfone in combination with streptomycin, dihydrostreptomycin, and isonicotinic acid hydrazide. Both the pulmonary lesions and the lesions of tuberculoid leprosy greatly and immediately improved. Tests of the nasal mucus and of exudates of the nodular lesions of leprosy became negative for M. leprae. The patient gained weight, her general condition rapidly improved, and she seemed to be on the way to complete recovery.

Inflammatory "Ringworm." R. J. Rowe. Wisconsin M. J. **57**:115-117 (March) 1958 [Madison].

The author reviews observations on 58 patients with inflammatory ringworm seen over a period of 6 years at the Marshfield Clinic, in a rural region of Wisconsin, where the condition is rather common. The infection is called "kerion" when it appears on the scalp and "tinea barbae" when it appears in the bearded area; the term "tinea profunda" is sometimes used to describe the disease occurring in other areas of the body. The ages of the patients ranged from 2 months to 62 years. There were 39 males and 19 females. Among the 32 patients less than 14 years of age, there was an equal number of boys and girls, but among those over 14 years, there were only 3 females. The disease is thought to be contracted from animals but not to be infectious from one person to another. Men have more exposure than women as age progresses. The adult scalp resists ringworm infection, but the male beard is very susceptible. Erythema and scaling are the first signs of infection. If the involved areas become edematous, the physician should warn his patient that the "deeper," more inflamed type of ringworm may be present. The infection often progresses to form a nodular, boggy area with many draining sinuses. Even though fluctuation is present, attempts to incise and drain the nodules are often not successful because of the boggy nature of the tissue. Hair in the area tends to break off and may be pulled with ease. Enlarged, tender, regional lymph nodes are usually present. Not infrequently the temperature is elevated, and occasionally a generalized papuloerythematous eruption appears (trichophytid). The disease runs its course in 2 to 4 months but may last longer.

At least in the early stages, the inflammation seems to be primarily an allergic reaction to the tinea. When pustules and drainage occur, secondary bacterial infection may be present. A diagnosis can be established by placing scales of hair from the involved area on a slide, applying a drop of 15% potassium hydroxide solution, then a cover slip, heating to just below the boiling point, and then exerting pressure on the cover slip. If spores or mycelia are present, a positive diagnosis can be made, but the converse is not necessarily true. Particularly in the later stages of the infection it may

not be possible to demonstrate spores or mycelia. In the author's series microscopic examination was not performed in all cases, but mycelia or spores were found in 38 of the 58 patients. Cultures were done in 22 of the cases. Trichophyton gypsum was identified in only 4 cases. T. verrucosum frequently causes ringworm in cattle, but the author used Sabouraud's medium, on which T. verrucosum does not grow well. Since fungicidal drugs are largely ineffective, treatment is mostly palliative. During the acute draining stage, hot, wet compresses dipped in Burow's solution should be applied 3 times daily. On the scalp the author uses 1% iodochlorhydroxyquin (Vioform) 3 or 4 times daily. On other areas 1% hexachlorophene in calamine liniment is useful. As the drainage subsides, 2% iodochlorhydroxyquin in yellow petrolatum is applied 3 times daily. This therapy helps to prevent secondary infection.

Molluscum Pseudocarcinomatosum. F. Linell and B. Månsson. Nord. med. **59**:226-227 (Feb. 6) 1958 (In Swedish) [Stockholm].

Molluscum pseudocarcinomatosum develops rapidly. In 2 to 6 weeks a cupola-formed skin tumor can develop, as a rule 10 to 20 mm. in diameter, 5 to 10 mm. in height, having in the center a corneous plug. Regression is followed by expulsion of the plug. Healing leaves a more or less conspicuous scar, depending on the degree of secondary infection. There is a great resemblance to squamous epithelial carcinoma. The sites of predilection are the face and hands. The etiology is unknown. The localization to exposed cutaneous areas suggests exogenic influence. In the 10-year period from 1945 to 1954, 533 cases of squamous epithelial carcinoma were registered in the Radiologic Clinic in Lund. On follow-up 99 were diagnosed as molluscum carcinomatosum. The clinical picture was typical of molluscum carcinomatosum in additional cases, but the histological material was insufficient for confirmation of the diagnosis. Abundant biopsy material is necessary to allow a definite diagnosis by comparison of the clinical picture and the histological picture. Two-thirds of the patients with this disorder were men. The average age for both men and women was 59, or about 10 years younger than that for squamous epithelial carcinoma. With purely conservative treatment the cosmetic result is often unsatisfactory. Since 1955 the technique described by Beare and others has been applied in Lund. The tumor is planed off even with the skin surface and the bleeding stilled by thermocautery. Abundant biopsy material for histological examination is thus obtained. If the diagnosis is confirmed histologically, no further measures are taken and excellent cosmetic results have been attained. If squamous epithelial carcinoma cannot be excluded, radiologic treatment is given. The practical consequences of distinguishing molluscum carcinomatosum from squamous epithelial carcinoma are stressed.

Contact Dermatitis from "High-Speed-Duplicator" Papers: A New Disease of Office Workers. C. Sheard Jr., H. J. Spoor and R. Abel. A. M. A. Arch. Dermat. **77**:435-437 (April) 1958 [Chicago].

The authors present the histories of 5 patients with an unusual type of contact dermatitis affecting the lips, eyelids, and fingers of office workers. The cause is a type of sensitized paper used in a new high-speed duplicating machine in which the paper is inserted in the machine, along with the sheet to be copied, and is exposed to intense light. The chemical in the paper is a trade secret. Speculation suggests that it is a phenolic compound. The authors strongly suspect that it may be closer to the photodevelopers, such as *p*-methylaminophenol sulfate (Metol). The eruption is severe, with visiculation, erythema, and seborrhea-like superficial scaling. It characteristically seems to involve the lower lip in smokers and is pruritic and annoying. Messengers exhibit the rash on the knuckles where they contact the paper when they carry bundles of it, with fingers under the string; in businessmen the dermatitis often develops on the first 3 fingers, with which they touch the paper when turning pages, or on the right palm, when they are making notes. Since there is no known method of desensitization, cure can be attained by a change of job or a change of paper. Hypoallergic or nonallergic papers are available for some types of duplicators. The described cases of contact dermatitis suggest that, as more chemically treated substances come into common use, obscure skin conditions will continue to arise and require detailed history-taking for proper discovery and cure.

INDUSTRIAL MEDICINE

Observations on the Course of the Recent Influenza Epidemic and on Its Preventive and Therapeutic Treatment in a Factory Community. C. Rotta. Minerva med. **49**:329-337 (Jan. 31) 1958 (In Italian) [Turin, Italy].

The author presents 3 observed phases of an influenza epidemic in a factory community in the fall of 1957: incidence of the epidemic among nonvaccinated children; effect of influenza vaccination in a factory community; and results of preventive and therapeutic treatment of children with influenza by using the serum of convalescents from influenza. Influenza spread among all 1,000 nonvaccinated boys, between the ages of 6 and 12 years, in a children's community center. Most children became ill between the 6th and the 11th day of the epidemic. Mean duration of the disease was

from 5 to 6 days. The onset of influenza was sudden and was marked by high fever, headache, malaise, chilliness, and muscular and joint pains. Inflammation of the respiratory tract and gastrointestinal disturbances appeared a few days later. General health remained good, even in the more severe instances. The disease relapsed in 134 children (13.4%). All 200 adults working in the community center also became ill with influenza. The disease did not differ between adults and children either in duration or in symptoms. The considerably higher incidence (4-5 times) of the disease among adults working in the community center, as compared with adults not connected with the center, indicates that during severe epidemics of influenza the length of time exposure to the infectious agent has more weight than individual defensive stamina.

During the same period of the influenza epidemic a study was made on 8,618 factory employees, mostly males, of whom 4,776 were plant workers and 3,842 office employees. They were divided into 2 equal groups, 1 of which received a polyvalent vaccine against influenza and the other constituted the control group. In the vaccinated group, 470 plant workers (19.7%) and 249 office employees (13%) became ill with influenza. In the control group, 551 plant workers (23%) and 487 office employees (25%) became ill. To summarize, 719 of all vaccinated employees (18.7%) and 1,038 of nonvaccinated employees (23%) contracted the disease. There was also a slightly higher incidence of the disease among the plant workers than among the office employees. Vaccination resulted in a lower incidence of the disease and in a lower absenteeism from work.

Serum of convalescents from influenza was administered intramuscularly in doses of 2 to 8 cc. to another group of children as a prophylactic agent. Symptoms were milder and were accompanied by only a slight fever in children who received the serum and became ill as compared with ill children who did not receive the serum. Serum of convalescents from influenza administered to other children with the acute type of the disease brought about a rapid improvement and gradual remission of symptoms. Serum of convalescents from influenza thus has proved to have a certain therapeutic value.

THERAPEUTICS

Spleno-Portal Route in the Treatment of Liver Disease. G. Scevola. Gazz. med. ital. **117**:56-62 (Feb.) 1958 (In Italian) [Turin, Italy].

The splenoportal route is presumably an efficacious route for drug administration in the treatment of liver disease because of its anatomic proximity to the liver. The author observed the therapeutic effect of an Italian proprietary preparation of inositol, administered by the splenoportal route to 35 rabbits in which hepatic damage was experimentally produced. Carbon tetrachloride, the toxic substance, was given to all animals in a total dosage of 7.5 cc. per gilogram of body weight for a period of 10 days. Thirty rabbits, which were divided into 3 equal groups, received inositol for 10 days. The first group was given the drug orally in daily doses of 0.50 Gm. per kilogram of body weight. The second group was given the same amount intravenously. The third group was given the drug by the intrasplenic route in daily doses of 0.25 Gm. per kilogram of body weight. The spleen was exteriorized and fixed subcutaneously in order to facilitate repeated injections of inositol into it. Specimens of liver were obtained from the animals by biopsy before and after medication with inositol. A fourth group, consisting of 5 rabbits which were used for control purposes, was given no medication. Liver material was obtained from this group by biopsy at the end of the intoxication and 5 days later.

The rabbits were weighed during the periods of intoxication and medication. They decreased in weight about 200 Gm. per kilogram of body weight during intoxication. They also lost appetite and vivacity. Gradual improvement of these conditions was observed during the period of recovery, and it was more marked in the animals which had received inositol than in those in the control group. Histological examination of liver specimens showed a slightly greater effect of the drug administered by the oral or intravenous route than by the splenoportal route. However, the amount of the drug administered by the splenoportal route was equivalent to half of the amount given by either of the other 2 routes. Two hypotheses may be drawn from the histological findings. One is that the splenoportal route is more efficacious than the oral or intravenous route. The other is that the drug given by the splenoportal route passes unabsorbed through the liver and then returns to it with the arterial blood to be eventually metabolized there.

The Fluid and Electrolyte Therapy of Severe Diabetic Acidosis and Ketosis: A Study of 29 Episodes (26 Patients). H. E. Martin, K. Smith, and M. L. Wilson. Am. J. Med. **24**:376-389 (March) 1958 [New York].

The authors report on 16 female and 10 male patients, between the ages of 14 and 73 years, with severe diabetic acidosis and ketosis who were treated at the Los Angeles County Hospital. Three of these patients had 2 attacks of severe diabetic ketoacidosis. Three types of repair fluids of varying tonicity (hypotonic, isotonic, and hypertonic), containing molar sodium lactate, a modified Butler's solution (containing 57 mEq. of plasma electrolytes), and sodium chloride solution, were used with some variation among the patients. Potassium

chloride and potassium phosphate were given in various amounts, as indicated in the results. All the patients received 200 units of regular insulin intravenously every 2 hours until the blood sugar was below 300 mg. per 100 cc., when smaller doses were given intramuscularly at 2- to 4-hour intervals. Seven of the 26 patients died, representing a mortality rate of 24%. Three of the deaths were clearly not due to the diabetic ketoacidosis.

An attempt was made to evaluate, with balance studies, the various types of repair fluids used. There was little difference in the volume of fluid retained. Hyperosmolarity of the serum was present in 14 (52%) of the 26 patients on admission and in 12 (46%) of the patients after 12 hours of therapy. When hypertonic fluids were used, there was more hyperosmolarity of the serum after 12 hours of therapy than with hypotonic fluids, and hypernatremia and hyperchloremia were frequently noted. This indicates the need for use chiefly of hypotonic fluids. Factors influencing the correction of acidosis included the lactate/chloride ratio of the intravenously administered fluid used (considered to be best at a ratio over 1.0), the serum chloride level on admission, the use of hypertonic solutions, the large loads of 0.9% sodium chloride solution, and the rate of fall of the blood ketone levels. Detailed balance studies in 8 patients correlated well with previous estimates of 5 to 10% body fluid loss and with balances of certain ions. It is believed that the average range of intake in the early, more acute phases of treatment should be 70 to 120 cc. of water per kilogram of body weight, 7 to 10 mEq. of sodium per kilogram, 5 mEq. of chloride per kilogram, 2 to 3 mEq. of potassium per kilogram, 0.2 mEq. of magnesium per kilogram, 1 mM. of phosphorus per kilogram, and 4 to 5 mEq. of bicarbonate radical per kilogram.

Treatment of Bronchial Asthma with Aerosol of Prednisolone. G. Massara and G. P. Teatini. Minerva med. 49:550 (Feb. 17) 1958 (In Italian) [Turin, Italy].

Inhalation therapy with an aqueous solution of aerosol of prednisolone, dissolved in a concentration of 0.25%, was given to 20 patients with bronchial asthma. Most of the patients, who were below the age of 40 years, complained of intense dyspneic episodes, particularly at night, accompanied by cough and expectoration of sputum. Three patients, who were over 40 years of age, with a chronic type of bronchial asthma, had a painful but not severe dyspnea; on roentgenologic examination a pulmonary emphysema without involvement of the cardiovascular systema was established. The initial daily dosage to all patients consisted in the inhalation of 5 mg. of prednisolone. The dosage was efficacious in 14 patients and caused diminution of the symptoms already on the 4th or 5th day of medication. The dosage was doubled in the remaining 6 patients to 10 mg., and it was given once a day or divided in 2 daily doses. Improvement in symptoms was observed in 5 patients. The therapy was ineffective in 1 patient who had a state of recurring dyspnea. The treatment was well tolerated by all patients.

The advantage of inhalation therapy with aerosol of prednisolone over either oral or parenteral route consists in the possibility of using a lower dosage of the drug, which lessens the incidence of side-effects. Aerosol therapy with prednisolone can thus be used effectively in maintenance therapy with prednisolone. Unfortunately, the effects of inhalation therapy with aerosol of prednisolone, like those of prednisolone administered orally or parenterally, vanish soon after discontinuance of the therapy. Symptoms of the disease recurred in all patients in this series within 2 to 4 days after discontinuance of the treatment. The inhalation route is also less comfortable than the oral. The quality of solubility of prednisolone increases its therapeutic value; intravenous administration of prednisolone, combined with the aerosol therapy, can promptly produce a high blood concentration of prednisolone, which procedure is required in some instances.

An Evaluation of Drug Therapy in Hypertension. J. D. Dorsett Jr., J. W. Woods, K. L. White and others. J. Chron. Dis. 7:287-299 (April) 1958 [St. Louis].

Nine men and 7 women, between the ages of 32 and 55 years, with essential hypertension were studied, with particular emphasis on evaluation of the response of their blood pressures to 4 therapeutic regimens, namely, placebo, phenobarbital, reserpine, and reserpine combined with hydralazine. Most of the patients had pressures in excess of 200/110 mm. Hg. The 16 patients were distributed among 4 groups of 4 persons each, so that the patients in each group had about similar blood pressures and "social stress" ratings in order to balance out the influence on therapy of such factors as marital and domestic strife. In order to observe and control as many variables as possible, double-blind techniques were used. The patients within each group were assigned to treatments at random by the biostatistician who had never met the patients and knew the 4 regimens only by the letters A, B, C, and D. One of the authors saw the patients at weekly intervals for 32 weeks, but blood pressures and therapeutic regimens were unknown to him and the patients until the end of the 32-week period. The other authors were aware of both blood pressures and drugs given the patients and had over-all supervision of patient care.

In all patients who received reserpine combined with hydralazine, both systolic and diastolic blood pressures fell during the treatment period. The average decrease for this group was 43 mm. Hg systolic and 32 mm. Hg diastolic. In all 4 patients

the systolic and diastolic pressures rose in the final control period when the combined administration of the 2 drugs was discontinued. For patients with moderately severe hypertension the combination of reserpine and hydralazine thus was a hypotensive agent of considerable potency. The decrease in blood pressure observed in the patients who received reserpine alone was not considered important when subjected to statistical analysis. The accelerated phase of hypertension occurred in 2 of the 4 patients who were given phenobarbital, and these 2 were dropped from the study. Of the other 2 patients in this group, 1 had a slight rise in pressure, and retinal hemorrhages and exudates occurred. The blood pressure of the 4th patient remained essentially unchanged. The results in the phenobarbital group illustrate the difficulty in evaluating hypotensive agents even when great efforts are made to control some of the factors which might otherwise account for differences in patient responses. They also emphasize the unpredictability of the natural course of essential hypertension in the individual patient. There was no appreciable change in blood pressure in those patients who received only placebo. No conclusions are drawn concerning the possible effect of the drugs tested on the natural history of essential hypertension or the prognosis of the disease.

958
167

Aplastic Anemia After Myleran Treatment in Chronic Myeloid Leukemia. J. G. M. Van Esser. Nederl. tijdschr. geneesk. **102**:379-381 (Feb. 22) 1958 (In Dutch) [Amsterdam].

The author presents the histories of 2 patients who were treated with busulfan (Myleran) for chronic myeloid leukemia. The first patient had taken 4 mg. of busulfan daily for several months and then 2 mg. daily for 1 month, a total of 364 mg. The second patient had taken 2 mg. daily for 7 months. A hemorrhagic tendency developed in both patients, and aplastic anemia was detected. Repeated transfusions of fresh blood were given to counteract the anemia. These were tolerated at first, but both patients died of cerebral hemorrhage. The author emphasizes that control studies should be made on all elements of the blood at regular intervals during busulfan therapy and for several months after the discontinuation of this therapy.

Treatment of Paralytic Ileus with Cholinesterase Inhibitors in Intravenous Drip. U. Breine, I. Hedenberg, and S. O. Liljedahl. Acta chir. scandinav. **114**:172-180 (No. 3) 1958 (In English) [Stockholm].

Fifty patients with paralytic ileus were treated with cholinesterase inhibitors administered by intravenous drip at the Lidköping Hospital in Sweden. Two proprietary preparations of neostigmine in doses of 2 to 4 mg. in 1 liter of dextrose, invert sugar, sodium chloride solution, or a 6% colloidal infusion solution with 0.9% sodium chloride (Macrodex), were given at the usual drip rate of 30 to 35 drops per minute. The patient received the intravenous neostigmine drip for 24 to 48 hours and in exceptional cases for longer periods. A radiographic contrast medium was given a few hours before the drip was instituted in order to make sure that the contrast medium had started to pass from the stomach to the intestine so as to prevent the entire gastric contents being removed from the stomach by vomiting. The patient usually had an indwelling duodenal catheter.

In some patients, intestinal function started after 2 or 3 hours, and in others after about 24 hours; it appeared to be marked in both the large and the small intestine. In only 1 patient who was in poor condition did the neostigmine drip fail to produce any effect. No great discomfort was reported by the patients. No undesirable side-effects were noted except in 1 patient in whom nausea required discontinuation of the drip. No cardiovascular complications occurred. The threshold for intestinal stimulation appears to be appreciably lower than that for cardiac stimulation.

The intravenous administration of cholinesterase inhibitors is indicated chiefly in paralytic ileus and in combinations of this form of ileus with mechanical intestinal obstruction. Cholinesterase inhibitors are contraindicated in the presence of strangulation of the intestine. The stimulating effect of neostigmine on the intestinal activity may be attributed to an increased acetylcholine action on the intestine. In view of the difficulty familiar to the surgeon and the roentgenologist of accomplishing adequate decompression, which is an essential part of the treatment of intestinal obstruction, with an intestinal catheter, the technique of intravenous administration of a cholinesterase inhibitor appears to offer appreciable advantages. Neostigmine drip combined with a contrast meal is also a valuable aid in differentiating between paralytic ileus and partial mechanical obstruction.

Cycloserine-Isoniazid Combination Therapy in Virgin Cases of Pulmonary Tuberculosis. I. G. Epstein, K. G. S. Nair, L. J. Boyd and P. Auspitz. Dis. Chest. **33**:371-381 (April) 1958 [Chicago].

Fifty-five men and 26 women, between the ages of 17 and 73 years, with recent pulmonary tuberculosis, who had not been treated previously, were given capsules containing 0.5 Gm. of cycloserine (Seromycin) and 0.3 Gm. of isoniazid daily; the drugs were administered orally in 2 divided doses, morning and evening, for 6 to 16 months. A chest roentgenogram was taken monthly, bacterial examination of the sputum was made bimonthly by smear and culture, and, when negative, examination of the gastric contents was made. Cycloserine

plasma levels were obtained at regular intervals. Liver and kidney function tests and peripheral blood studies were also done several times in the course of the therapeutic trial. Sixty-eight (84%) of the 81 patients had some degree of fever, and all the sputums were positive for tubercle bacilli on smear, and confirmed by culture.

Clinical improvement, drop of temperature, lessening of the volume of sputum, and gain in weight occurred promptly in every patient. The administration of a single capsule containing cycloserine and isoniazid was more acceptable to the patients than the usual isoniazid-aminosalicylic acid (PAS) combination. Within 6 weeks, 40% of the chest roentgenograms showed evidence of improvement. The figure rose to 74% in 12 weeks, and it reached 93% for 48 patients treated for 6 months. Evidence of reduction in the bacillary content of the sputum was obtained within 6 weeks of treatment. Within 3 months 80% of the sputums obtained from 64 patients were negative on culture, and at 6 months the figure rose to 87%. Bacillary sensitivity to cycloserine fell slowly and slightly during prolonged treatment with doses of 1 Gm. or more of cycloserine per day. With the daily dose of 0.5 Gm. of cycloserine, there was no evidence of decreased sensitivity. Resistance to isoniazid developed during the administration of the cycloserine-isoniazid compound at about the same rate as was observed when isoniazid was given alone. An untoward reaction occurred in only 1 patient and did not necessitate discontinuation of the treatment. A combination of 0.25 Gm. of cycloserine and 0.15 Gm. of isoniazid given twice daily is to be considered effective and safe therapy against pulmonary tuberculosis in patients previously untreated. The clinical results obtained were superior to those usually obtained from isoniazid-aminosalicylic acid therapy, both in speed and in degree of response, as gauged by changes in the chest roentgenograms and sputum conversion.

Anticoagulant Treatment of Postoperative Venous Complications. M. Alonzo. Riforma med. **72**:120-126 (Feb. 1) 1958 (In Italian) [Naples].

One hundred twenty patients with postoperative venous thrombosis or pulmonary embolism were treated with anticoagulants. Varicose phlebitis of the legs and superficial phlebitis of the saphenous vein were present in 15 patients. The disorders were corrected by the use of anticoagulants. Thrombosis of the deep veins of the calf developed in 40 patients and was corrected by prompt administration of heparin. A mild edema, which appeared in most patients, subsided within 3 to 4 days; the patients were able to leave the bed after 4 to 5 days. Thrombosis of the thigh, which developed in 15 patients, required anticoagulant therapy for 15 days. Thrombosis of the iliac vein developed in 5 patients, was more difficult to treat. Complications associated with this disorder were frequent, and there was also a hazard of involvement of the vena cava. Thrombosis of the vena cava developed in 1 patient and required treatment with heparin for 25 days. Venous thrombosis associated with arteriospasm developed in 2 patients. This disorder was effectively treated by a combination of procaine hydrochloride and heparin. Phlebitis of the arm, which developed in some patients, was easily managed. Embolism of the pulmonary artery, which affected other patients in this series, required prolonged anticoagulant therapy. Procaine hydrochloride, papaverine, cardiac tonics, and oxygen were added to heparin for the treatment of this complication.

Dark skin pigmentation and permanent edema were the most common sequelae observed. They were due to too late institution or too early withdrawal of anticoagulant therapy. Hemorrhage occurred in only 1 patient. It developed in a woman, 20 years old, who before admission to the hospital had taken 20 tablets of Dicumarol on the erroneous impression of taking a tonic treatment. Hemorrhage was corrected with considerable difficulty. The author believes that anticoagulant therapy is the most important aid in controlling postoperative venous complications. Selection of the right dosage is essential because of the narrow margin between the therapeutic dosage and one producing hemorrhage.

PATHOLOGY

Abnormal Entering of All Pulmonary Veins into the Left Innominate Vein, with Interatrial Communication (Taussig-Snellen-Albers Syndrome). I. Ferrario. Schweiz. med. Wchnschr. **88**:256-261 (March 15) 1958 (In German) [Basel, Switzerland].

The author reports on a 4½-year-old girl and a 10-day-old boy with abnormal entering of all pulmonary veins into the left innominate vein, combined with an interatrial septal defect but without any other major cardiac malformation. The term "Taussig-Snellen-Albers syndrome" is suggested for this malformation of the pulmonary veins. The chest roentgenogram of the girl showed the typical figure-8 shape, formed by the widened shadow of the upper mediastinum and the enlarged cardiac shadow. The death of this patient resulted from acute pulmonary edema, since failure of the right ventricle had its repercussions in the lesser circulation. Autopsy was performed and revealed a common vertical ascending venous trunk on the left side, through which the pulmonary veins entered the innominate vein. The boy died in a hypoxemic state caused by pronounced pulmonary congestion due to stenosis of a common ascending pulmonary

artery on the left side, through which the pulmonary veins entered the innominate vein, as revealed by autopsy. Of 22 patients with congenital malformations of the heart and the large vessels, who died in the course of the first 6 months of 1957 and on whom autopsies were performed at the pathological institute of the University of Zürich, only these 2 patients had the Taussig-Snellen-Albers syndrome. Fifty-seven similar cases were collected from the literature, in 35 of which the diagnosis was established at autopsy and in 6 at surgical intervention; in 16 cases a clinical diagnosis was made with the aid of cardiac catheterization and angiocardiography.

Pathogenetically, this malformation is due to an arrest of growth of the sinoatrial region at the end of the first month of embryonic life, either with lack of formation or with secondary closure of a connection between the pulmonary venous system and the heart. As a consequence, persistent anastomosis between the plexus pulmonalis and a remainder of the left vena cardinalis cranialis (left vena cava superior) occurs from which the truncus venosus communis develops. There is hypoplasia of the left atrium, hypotrophy of the left ventricle, and hypertrophy of the right ventricle resulting from the extra load placed on the heart. Occasionally, the additional load placed on the pulmonary circulation may cause thickening of the media of the small pulmonary arteries. In the reported case of the girl, a congenital pericardial diverticulum of the posterior wall was detected, an interesting embryologic condition. The clinical diagnosis of this syndrome may be presumed by the figure-8-shaped chest roentgenogram. Other symptoms observed are dyspnea on exertion, cyanosis, pulmonary congestion, with frequent bronchopneumonia and progressive heart failure. Electrocardiograms show hypertrophy of the right ventricle, sometimes also hypoplasia of the left ventricle. The diagnosis must be confirmed by angiocardiography and catheterization of the heart. The prognosis depends on the possibilities of compensation of the right ventricle. According to the cases collected from the literature attempts at surgical intervention in this type of malformation have failed.

Histological and Histochemical Changes of Rat's Sarcoma in the Process of Its Cure by Sarcolysin and Dopan. L. F. Larionov and M. A. Presnov. Arkh. pat. **20**:32-39 (No. 1) 1958 (In Russian) [Moscow].

Transplantable spindle-cell sarcoma (sarcoma 45) of rats was completely cured by new antitumor preparations—Sarcolysin [dl-p-di (2-chlorethyl) aminophenylalanin] and Dopan [2.6-dioxy-4-methyl-5-di (2-chlorethyl) aminopirimidin]. Pronounced changes were observed in the effect of Sarcolysin on the parenchyma as well as on the stroma of the tumor. The first signs of injury to the tumor were decrease of mitotic activity and disintegration of the nuclei of certain cells with formation of lumps. Later the size of the remaining cells considerably increased, their nuclei and nucleoli became larger, cells with numerous nuclei appeared, the fat was revealed in the cytoplasm, while the ribonucleic acid disappeared.

The injured cells were subjected to lysis. The process of healing included development of a large number of collagen fibers with disappearance of argentophilic fibers. The alkaline phosphatase activity increased during the process of treatment, first in the injured cells and later in connective tissue stroma of the tumor. The change in the parenchyma, i. e., of the tumor cells, is probably the primary factor in the process of cure, while the stroma reaction is secondary. However, the latter promotes the healing. Disturbance of nucleoprotein metabolism, especially in the nucleus, plays an important role in the mechanism of the therapeutic action of Sarcolysin and Dopan on the tumor.

Primary Hyperparathyroidism (Recklinghausen's Osteitis Fibrosa Cystica). J. Lauweryns. Belg. tijdschr. geneesk. **14**:1-16 (Jan. 1) 1958 (In Flemish) [Leuven, Belgium].

The clinical picture of hyperparathyroidism varies. When the patient is first seen, the physician may think of osteomalacia, osteomyelitis, skeletal carcinomatosis, chronic arthritis (senile, postmenopausal), secondary hyperparathyroidism with renal osteodystrophy, nephrolithiasis, Paget's disease, multiple myeloma, or polyostotic fibrous dysplasia. The histopathological picture of hyperplasia and of adenoma of the parathyroids is described, particularly with regard to differential diagnosis. The author prefers the term "metastasizing adenoma of the parathyroid" over "parathyroid carcinoma." The symptomatology is discussed with regard to the skeletal, hematological, urinary, gastrointestinal, and vascular systems. The histories of 3 patients with primary hyperparathyroidism are presented. The first patient had pure hyperplasia without the classical symptoms of osteitis fibrosa cystica generalisata but with scleroderma. The second and third patients had trabecular and medullary adenoma, respectively, with the clinical aspects of Recklinghausen's osteitis fibrosa cystica.

RADIOLOGY

Bronchiolar-Cell Carcinoma. J. H. Woodruff Jr., R. E. Ottoman and F. Isaac. Radiology **70**:335-348 (March) 1958 [Syracuse, N. Y.].

Bronchiolar carcinoma is different from bronchogenic carcinoma. The authors report 16 cases to illustrate the various features of the condition and cite observations by other investigators. The most common synonyms for bronchiolar carcinoma are

alveolar-cell carcinoma, pulmonary adenomatosis, papillary adenocarcinoma, and mucous carcinoma; others are primary multiple carcinoma, multicentric papillary adenocarcinoma of the lungs, columnar-cell carcinoma, alveolar-cell tumor, malignant adenomatosis, and multiple nodular carcinoma. Bronchiolar carcinoma is a primary lung tumor probably originating in the terminal bronchioles in the peripheral portions of the lung. It is composed of tall columnar or cuboidal mucus-secreting cells lying on an intact alveolar septum. It does not, as a rule, destroy the normal pulmonary tissue. The authors are making no distinction between this tumor and pulmonary adenomatosis. The distinctive histological pattern and pathogenesis set this tumor apart from other pulmonary neoplasms. These tumors are usually found in the peripheral portion of the lung; rarely major bronchi may be invaded late. There are no favorite sites. The tumors may be multiple or solitary, varying in size from those measuring a few millimeters in diameter to tumors involving the whole lung. A large mass may be present in 1 section, and multiple small nodules may be found in another section or sections. Metastatic spread by extension to contiguous areas, by the lymphatics and by the blood stream, are well established.

The ages of the 16 patients presented by the authors ranged from 33 to 83 years. A tabulation, in which the various aspects of bronchogenic and bronchiolar carcinoma are compared, shows that the sex incidence of bronchiolar carcinoma is about equal, whereas bronchogenic carcinoma predominates in males. In summarizing the radiologic features of bronchiolar carcinoma, the authors emphasize among other factors that the shadows vary considerably in size. At first they are small and faint, but they tend to grow persistently and progressively. As this occurs, their density increases. The initial roentgenologic finding may be a solitary nodule or infiltrate, a localized cluster of small densities, or diffusely scattered shadows throughout the lung. The shadows tend to combine to form larger "coin," pneumonic, or mass lesions. The margins of the shadows vary from fairly sharp to very indistinct. Dissemination to the same or the contralateral lung is common. In some patients lesions are disseminated on the first examination. Pleural effusions may obscure the primary lung tumor. They may occur on the homolateral or the contralateral side. The shadows may appear to clear at times as their pneumonic or focal atelectatic components resolve. The character of the primary and secondary lesions is not necessarily the same, as one may be nodular and the other infiltrative. While mediastinal adenopathy is discovered on pathological examination in 25% of the patients, it is not common in radiographic studies. Early localized lesions are best treated by resection of the lesion. Radiation therapy has been tried, but, in general, results have been discouraging. The need for early radiologic diagnosis is emphasized. Persistent nonregressing shadows and all mass lesions deserve study by cytological examination, bronchoscopy, bronchography, biopsy possibly by aspiration, and exploratory thoracotomy.

Erosive Rib Lesions in Paralytic Poliomyelitis. C. Bernstein, W. D. Loeser and L. E. Manning. Radiology **70**:368-372 (March) 1958 [Syracuse, N. Y.].

The authors call attention to erosive rib lesions which they observed in chest films of 14 of 28 patients with paralytic poliomyelitis, who were being studied at a respirator center. These rib changes did not occur earlier than 10 months after the onset of paralysis, were most frequently seen after 20 months, and in 1 instance did not appear for 45 months. The 3rd rib was involved most frequently, but the 2nd, 5th, 7th, and 8th ribs also showed similar lesions. Localized shallow indentation and narrowing of the upper rib margin were initially noted, progressing without regeneration or other signs of healing to almost total disappearance of bone structure. The rib lesions were unrelated to the age or sex of the patient, to type of therapy, or to presence of decubitus ulcer. No clinical signs or symptoms were attributable to the rib involvement. The most severely paralyzed patients showed the greatest frequency of rib involvement. In view of the localization of the rib erosion, continued pressure of the medial margin of the scapula against the posterior aspect of the rib appears to be the causative factor, although the reason for some patients being spared is not yet determined.

A New and Simple Approach to Air-Contrast Studies of the Stomach and Duodenum. K. Amplatz. Radiology **70**:392-394 (March) 1958 [Syracuse, N. Y.].

Various methods have been tried to produce double-contrast studies of the stomach and duodenum, such as the use of effervescent powders and carbonated beverages, the conscious swallowing of air, the insufflation and inflation of the stomach by means of inserted tubes, and the utilization of the air physiologically present in the stomach. The author presents the "straw technique" as a simple approach to air-contrast studies. Only an ordinary drinking straw, either paper or plastic, which has been punctured midway to produce a small perforation, is necessary. By means of this device one obtains simultaneous aspiration of barium mixture and air when the opaque medium is sipped. The size of the perforation in the straw is an important factor. The hole should be very small to allow the formation of only tiny air bubbles within the contrast material. This will insure an easily swallowed bolus containing both air and barium. A larger perforation requires ex-

cessive effort on the part of the patient, and the end-results are less favorable, as a smaller amount of air actually is swallowed. A through-and-through perforation of the straw made with a very small sewing needle proved most suitable.

Usually sufficient air will have entered the stomach when the patient, in the upright position, has ingested 2 to 3 oz. of the medium. Certain conditions must be met in order to obtain good contrast films. With carbonated drinks or effervescent powders, the amount of gas liberated is not easily controlled, and frequently overdistention, with consequent obliteration of mucosal detail, occurs. The patient may inadvertently respond to such overdistention by eructation, resulting in complete loss of gas. With the "straw technique" only a moderate amount of gas is introduced into the stomach under fluoroscopic control. One need not be concerned about perforating an ulcer by excessive distention of the stomach. There is no dilution of the opaque medium. One of the chief advantages is that disturbing gas bubbles, which serve to distort the mucosal detail, are held to a minimum. In the past 3 years the author has found this simple and inexpensive procedure to be a most satisfactory approach to double-contrast studies of the upper gastrointestinal tract.

958
167

Pneumopericardium Following Sternal Bone Marrow Aspiration: A Case Report. J. L. Ackerman and J. W. Alden. Radiology **70**:408-409 (March) 1958 [Syracuse, N. Y.].

An 18-year-old woman with fever of undetermined origin was subjected within a week to 2 chest roentgenograms, neither of which revealed any abnormality. During a bone marrow aspiration of the sternum, which was performed 10 days later, the physician thought he had gone too deeply, but the patient exhibited no reaction. The attempt to aspirate marrow was unsuccessful, and the procedure was postponed until a later date. Another roentgenologic examination of the chest on the day after the attempted sternal aspiration disclosed pneumopericardium. Four days later air was still demonstrable along the left cardiac border. Eventually it disappeared completely.

ANESTHESIA

Hypothermia in the Treatment of Cerebral Tumours. C. B. Sedzimir and J. W. Dundee. J. Neurosurg. **15**:199-206 (March) 1958 [Springfield, Ill.]

This report is concerned with the use of hypothermia at the Neurosurgical Center in Liverpool, England. The aim was not simply to use hypothermia but to combine it with controlled hypotension (produced by ganglion blocking drugs) when required. Chlorpromazine, with or without meperidine and/or Phenergan, is used for preoperative medication. Light general anesthesia is induced with thiopental, the larynx is sprayed with 4% lidocaine, and oral intubation is carried out with a flexometallic tube. A large flow of nitrous oxide–oxygen (with a T-piece open-circuit apparatus) and ether is used for the first 10 to 20 minutes to aid the peripheral vasodilatation. Surface cooling is commenced, once the patient is asleep, by application of ice bags all over the body and by laying the patient on a large ice pack. The position of the ice bags is changed frequently, and the patient is tipped in the head-down position at regular intervals to promote redistribution of the cooled blood. The ice is removed at 33 to 31 C (91.4 to 87.8 F), depending on the build of the patient and the final temperature required. The after-drop usually varies from 1.5 to 3 C. Unless the temperature has fallen below 28 C (82.4 F), no attempts at rewarming are made at the end of the operation. When necessary, radiant heat is applied until this temperature is reached. In the absence of any active means of rewarming, the normal body temperature is usually reached within 12 hours of the end of the operation.

During the first few months hypothermia in the Liverpool unit was reserved exclusively for operations on patients with vascular lesions and highly vascular tumors, such as meningiomas and acoustic neuromas. With the passage of time it was induced in patients with practically any type of tumor above or below the tentorium in the presence of considerable or long-standing raised intracranial pressure. Of a total of 174 operations under hypothermia, 94 were for cerebral neoplasms. The operating time was shortened by about one-third. The ease with which it was possible to operate with greater precision and with minimal operative trauma to the brain and blood vessels was of even greater importance. This reduction in operative trauma and in the necessity for occluding cortical veins is regarded as the main reason for the low incidence of cerebral edema. Another advantage of operating under hypothermia has been the fall in the intracranial pressure with reduction of brain volume. Even in the presence of large neoplasms, advanced papilledema, and dulling of consciousness from increased intracranial pressure, the exposed dura mater was not tense. The brain did not bulge, it was frequently shrunken and dry, and the dissection of tumors did not necessitate the same amount of manipulation and retraction. No death was caused by hypothermia. Although the number of tumors operated on with the help of hypothermia is still small, the authors believe that in neurosurgery a moderate cooling to 28 to 30 C (82.4 to 86 F) is entirely safe and that this degree of cooling offers all the advantages of the method.

PHYSIOLOGY

Altered Circulation in the Bone After Distal Diaphysial Fractures of the Tibia: Experimental Studies. G. Fonda and L. Giordano. Minerva ortop. 8:589-592 (Dec.) 1957 (In Italian) [Turin, Italy].

Clinical experience has shown that it takes a longer time for consolidation of a bone fracture at the medial or lower third of the tibia than at other sites of the body. Some workers believe that this phenomenon is due to interruption of the nutrient artery, which is supposedly the sole blood conveyor to the medial or lower third of the tibia. The authors observed the reproductive process of vascularization in an artificially produced fracture at the lower third of the tibia in guinea pigs and arrived at a different conclusion. The bone fracture did not greatly alter the blood supply to the bone cortex and to the periosteum. Interruption of the nutrient artery did not discontinue the regular blood flow to the inner layers of the bony stumps. Blood flow could have been maintained only through a great number of anastomoses in the bony stumps, which are confluents to the network of the periosteum. It is more difficult to interpret the blood flow through the medullary vascular network. In view of the interruption of the nutrient artery, continuity between the medullary and epiphysial networks and the vessels of the bone cortex can be assumed. The authors believe that probably a similar reproductive process of vascularization in a fracture at the lower third of the tibia takes place in human beings.

Circulatory Physiopathology of Fractures: I. Vascular Alterations of Fractures of the Upper Limb. G. Fonda and L. Giordano. Minerva ortop. 8:593-595 (Dec.) 1957 (In Italian) [Turin, Italy].

The authors performed experiments on guinea pigs by producing artificial fractures at the medial third of the humerus and of the forearm. A vasodilating process occurred near the fracture site promptly after the induced fracture of the humerus. This process was evident in a lesser degree after the induced fracture of the forearm. No qualitative or quantitative alteration of circulation was seen in the bone or in the surrounding soft tissue. A varying degree in intensity of hyperemia, which appeared in the internal networks of the bone, was consistent with the relative abundance or scarcity of the normal physiological pattern of vascularization. Vasodilative reactions were followed by vascular regeneration. The new blood vessels ran a twisted and irregular course, which turned gradually parallel to the bone axis. The formative process of vascularization penetrated into the bone callus from the surrounding connective tissue and from the stumps. Vascularization of the stumps consisted mainly in the proliferation of the medullary network, whereas contribution of the diaphysial vessels was small. The new network in the periosteum tended to localize on the surface of the bone callus. The interosseous artery became the origin of a rich vascular network after the fracture of the forearm occurred. A parallelism between the development of the vascular pattern and the formation of the respective bone callus could not be traced. Fractures of the forearm caused a quicker and more marked appearance of hyperemia, as well as a richer reproduced vascular pattern, than other fractures. Consolidation of fractures of the forearm was also slower than that of other fractures. The opinion of the authors is that hyperemia and vascular regeneration are related to proliferation of the connective tissue rather than to formation of bone callus.

Circulatory Physiopathology of Fractures: II. Vascular Alterations of Fractures of the Lower Limb. G. Fonda and L. Giordano. Minerva ortop. 8:596-598 (Dec.) 1957 (In Italian) [Turin, Italy].

The authors made analogous experiments on guinea pigs, as reported in the preceding article. Artificial fractures were produced at the medial third of the femur and of the tibia. Vascular alterations in the thigh and in the leg consisted in an active hyperemia and in vascular regeneration. These changes occurred in the adjacent soft tissue, in the bone medulla, in the periosteum, and to a less extent in the diaphysial cortex. These processes were more intensive and took a longer time in the femur than in the tibia. Thirty days after the induced fracture the reproductive process of vascularization in the femur was fully developing, whereas in the tibia it reached the stage of stabilization.

Better conditions for vascular redevelopment were observed in the femur than in the tibia. During the process of vascular regeneration no avascular areas were noted in the region of the femur fracture, but they were noted in the case of tibia or upper limb fracture. This observation has indicated that the period of fracture healing is not directly related to the process of regional vascularization. Although conditions of vascular regeneration are better in the case of fractures in the thigh than in the arm, yet consolidation of a diaphysial fracture of the femur takes more time than consolidation of a humerus fracture. Consequently, it is not possible to establish a relationship between the time of the fracture consolidation and alterations in the regional circulation after the fracture. The interosseous artery participated in the vascularization process of the bone callus which followed fracture of the forearm. A homologous process was not evident in the vascularization process which followed fracture of the leg.

BOOK REVIEWS

The Neuroses and Their Treatment. Edited by Edward Podolsky, M.D., F.A.P.A., F.A.P.M. Cloth. $10. Pp. 555. Philosophical Library, Inc., 15 E. 40th St., New York 16, 1957.

There is so much difference of opinion among psychiatrists and so many facets to the total field of psychiatry that it is impossible to write a definitive textbook. For this reason, several monographs, such as this one, covering one aspect of the subject have been published. The editor has selected 40 contributors who have written about special phases of the neuroses. Although there may be some differences of opinion as to the wisdom of including some of these papers, the editor has chosen wisely for the most part. The papers deal with problems in childhood, various syndromes, and methods of treatment. Some of the authors have written in too great detail and with terminology which may be difficult for the general practitioner or the medical student. The book does not have an index, nor is there a bibliography for any one of the chapters. It is, however, authoritative for the fields it covers and is recommended for use by persons interested in the neuroses and their treatment.

958
167

Surgical Forum. Volume VIII: Proceedings of the Forum Sessions, Forty-third Clinical Congress of the American College of Surgeons, Atlantic City, New Jersey, October, 1957. Cloth. $10. Pp. 671, with illustrations. American College of Surgeons, 40 E. Erie St., Chicago, 1958.

This book is a continuation of the publication of brief communications presented in the sections referred to as the "Surgical Forum" that are now an established part of the Annual Clinical Congress of the American College of Surgeons. Most of the papers are excellent. They are brief and easily readable, and the discussions are all to the point. Pertinent bibliographies are included at the end of each presentation. The reports deal with shock; fluids, electrolytes, and parenteral nutrition; wound healing and infections; trauma, burns, and radiation injury; cancer; liver and biliary tract; pancreatitis; heart; pulmonary physiology, anesthesia, and thyroid gland; gynecology and obstetrics; neurological surgery; orthopedics; plastic surgery; and urology. Most of the reports are by younger men who are in training or have recently completed training, with older men as collaborators. Clinical experimental observations and animal experiments are often dealt with in the same report, and results of work in both clinical and laboratory aspects of the problems are presented in each of the major sections. The great significance of this volume, as of the previously published volumes, lies in the fact that an excellent summary of what is going on in experimental surgery and clinical investigation is made available. Moreover, in these forums, which are being received with increasing enthusiasm, the younger generation of surgeons is given an opportunity to be heard at a national level by a large and sympathetic audience. Not the least important aspect in this situation is the fact that by means of these forums these younger workers do not have to wait for long periods to be heard in person by large numbers of their colleagues from all over the country and by those older than themselves. The American College of Surgeons deserves great credit for affording these opportunities to the younger men.

Traquair's Clinical Perimetry. By G. I. Scott, M.A., M.B., F.R.C.S., Professor of Ophthalmology, University of Edinburgh, Edinburgh, Scotland. With foreword by Norman M. Dott, C.B.E., M.B., F.R.C.S., Professor of Neuro-Surgery, University of Edinburgh. Seventh edition. Cloth. $17. Pp. 333, with 280 illustrations. C. V. Mosby Company, 3207 Washington Blvd., St. Louis 3; Henry Kimpton (medical book department of Hirschfeld Brothers, Ltd.), 134 Great Portland St., London, W. 1, England, 1957.

When Traquair published the first edition of his "Introduction to Clinical Perimetry" in 1927, it quickly became the standard textbook on this subject in the English speaking world, being widely adopted by ophthalmologists, neurologists, and neurosurgeons. His concept of the visual field as "an island of vision in a sea of blindness," his graphic descriptions of the topography of that island, his promotion of the values of quantitative perimetry, and the lucid interpretation of perimetric and tangent screen findings served to make his book a classic in the field. Each subsequent edition showed further improvements, the sixth edition having appeared in 1949. Dr. Traquair died in 1954 at the age of 79. The present author has retained much of the original flavor of the previous editions but has brought the work up to date. He has emphasized the value of the confrontation test, rewritten the chapters on glaucoma and affections of the optic nerve and chiasm, and added some new illustrations. Some of the newer developments, such as flicker fusion fields, the use of luminous test objects by "dark light" perimetry, and the multiple-pattern method for quick screening, either are not mentioned or are briefly dismissed. Not as complete in this regard as Harrington's "The Visual Fields," issued by the same publisher, this new edition of Traquair's monumental treatise nevertheless deserves a prominent position in the library of every physician concerned with perimetry as a diagnostic and prognostic aid.

These book reviews have been prepared by competent authorities but do not represent the opinions of any medical or other organization unless specifically so stated.

QUESTIONS AND ANSWERS

PERSISTENT PYURIA FOLLOWING PROSTATECTOMY

To the Editor:—*A 75-year-old man has had pyuria (4+) ever since he underwent a transurethral prostatectomy a year ago. He has had only one febrile reaction since his operation. A stained smear of urine sediment revealed what appeared to be a gram-negative diplococcus, intracellular, resembling Neisseria gonorrhoeae very much. A pure culture of tribe Mimeae was reported. Bacterial sensitivity tests revealed that the organism was somewhat sensitive to antibiotics. Is there any drug that would have a specific effect on this organism and would be likely to eradicate it from the urinary tract?*

Hinton J. Merritt, M.D., Colquitt, Ga.

Answer.—The species Mimeae is, in essence, a gram-negative bacillus, but, because of bipolar staining, it may resemble a gram-negative diplococcus. There is no report that this organism is naturally sensitive to the antimicrobial agents, so it it likely that such resistance has been acquired. It is not uncommon after transurethral resection of the prostate for pyuria to persist indefinitely, and the urine can be cleared of pus only temporarily. Since this patient has had only one febrile reaction, the best management would be to forego any intensive therapy and to institute treatment only when he has some subjective symptoms, such as fever or dysuria. It is likely that one of the sulfonamides—even though the Mimeae are resistant in vitro—would control such symptoms, because of the higher concentration in the urine than in the serum.

ELECTRICAL CONDUCTIVITY OF BLOOD

To the Editor:—*Please give information relative to the conductivity and/or specific resistance of human blood.*

F. J. Kelly, M.D., Amarillo, Texas.

Answer.—The ability of a solution to conduct an electric current depends on the number of ions available in solution and on the velocities with which these ions move in the electric field. The specific resistance of a conductor is the resistance in ohms offered by a cube of the substance or solution 1 cm. long by 1 sq. cm. in cross section. The specific conductance is the reciprocal of the specific resistance and is expressed in reciprocal ohms or mhos. The specific conductance of human serum at 18 C is about 110×10^{-4} reciprocal ohms. The conductance of serum is a function of the number (per unit volume) and mobilities of all the ions present. There are additional factors which influence the conductance of serum. These are the total protein level, the pH of the serum, and the temperature. The relation between specific conductance and the "total base" of serums of varying protein content at a given temperature has been studied by Sunderman, who has derived a formula and chart relating these factors (*J. Biol. Chem.* **143**:185, 1942; *Am. J. Clin. Path.* **15**:219, 1945).

TIGHTNESS IN THE CHEST

To the Editor:—*A 35-year-old woman has been having "spells" which started about 14 months ago. Her symptoms at that time were "strange feeling and tightness" in her chest. These have become progressively worse, and new symptoms have appeared. The first addition was pain in her chest and, later, in both arms. The last episode, which was witnessed, occurred a few days ago, when she complained of feeling the pain in her chest and down her arms. Objectively, her superficial leg and arm veins were very much dilated. She said she also felt weak and faint. Her hands were dark red, almost cyanotic in appearance, and her feet were similarly discolored. These episodes have lasted from about 15 minutes to several hours. She is well between attacks. She had the book thrown at her in the laboratory and it came out second best—all findings in the tests were normal. The x-ray department reported a congenital heart defect, a patent foramen ovale. Her blood pressure is usually 100/75 mm. Hg; however, it has ranged down to 80/50 at times. She has been to several doctors and hospitals and no one can explain these bizarre symptoms. Please supply diagnostic assistance.*

M.D., Michigan.

Answer.—The sensations of pressure in the chest and the pains radiating down the arms seem to indicate that there is some cardiac disease. The clinical picture conforms with the description that one finds with coronary insufficiency. It is assumed that electrocardiograms did not show any abnormalities of the conductive system and that there are no abnormal findings in the lungs. However, the x-ray department did report a patent foramen ovale. The prominence and dilatation of the veins in the upper and lower extremities suggest some

The answers here published have been prepared by competent authorities. They do not, however, represent the opinions of any medical or other organization unless specifically so stated in the reply. Anonymous communications cannot be answered. Every letter must contain the writer's name and address, but these will be omitted on request.

embarrassment on the venous return involving the superior and inferior vena cava. Since this occurs at the same time, it may be assumed that the causative factor is where the cava are close together, which would signify the right auricle. The dilatation of the veins is probably not due to any involvement or disorder of the peripheral venous system. This would seem to be connected with some clinical disturbance of the normal cardiac function. It is difficult to decide whether it is due to a ball-valve embolus or possibly some tumor in the heart or other abnormality which is disturbing the normal cardiac function. The solution of the problem could be more definitely crystalized if this case were studied with the newer techniques in cardiology, namely, angiocardiography, catheterization of the heart, and an estimation of the oxygen content in the chambers. Investigation of the patent foramen ovale may throw further light on the problems. Management will depend on the results of the findings.

MEPHENESIN FOR MUSCLE PAINS

To the Editor:—*A 54-year-old woman feels fine all day, but as soon as she falls asleep she is suddenly awakened with pains (not cramps) in many parts of the skeletal area. She has been troubled this way for years. She is not neurotic. In order to relieve her distress, she arises and walks about, and she is immediately relieved. Since mephenesin preparations give more relief than anything else that has been tried, please give further information on this type of therapy.*

Horace A. Hall, M.D., Corona del Mar, Calif.

Answer.—Mephenesin (in the United States) or myanesin (in Great Britain) is an aromatic glycerol ether (3-o-toloxy-1,2-propanediol). Berger and Bradley (*Brit. J. Pharmacol.* 1:265, 1946) thought that, due to the depressant action of mephenesin on certain polysynaptic pathways in the spinal cord, skeletal muscular relaxation took place without loss of consciousness. Their work stimulated various investigators to study the diminution of skeletal muscular tone and involuntary movement in such conditions as muscle spasm of traumatic origin, rheumatic arthritis, tetanus, and various neurological hyperkinetic states. Reports of ineffectiveness of this drug have appeared, but there is evidence that it has been of some value in patients with hypertonus of skeletal muscle and spasticity. Domino, who has published the most recent comprehensive work on mephenesin and mephenesin-like substances, stated that mephenesin may be strikingly effective in some cases of spasticity and completely ineffective in others (*Ann. New York Acad. Sc.* 64:705, 1956). Thus, the transient duration of action of mephenesin and low order of potency when given orally do not produce uniformly effective results.

VASOSPASM OF THE RETINAL ARTERIES

To the Editor:—*A patient, 60 years of age, had a thrombosis of a branch of the left retinal artery 10 years ago and a thrombosis of branches of the right retinal artery 1 year ago and again one month ago. There has been no other evidence of vascular disease. The blood pressure, electrocardiogram, serum cholesterol level, and sedimentation rate are all within normal limits. Funduscopic examination of the uninvolved vessels revealed normality compatible with the patient's age. After the second thrombosis, therapy with bishydroxycoumarin was instituted; however, the prothrombin time was below therapeutic levels at the time of the last thrombosis. Could vasospasm be a primary or contributing factor in these multiple thromboses? If so, would papaverine hydrochloride, tolazoline hydrochloride, and/or other vasodilator drugs be of value? Please give further suggestions for therapy.* *M.D., New York.*

Answer.—Vasospasm, if not a contributing factor to thrombosis of retinal arterioles, is certainly an accompanying one. It is now felt that emboli almost never occur in the retinal arterial tree and that even primary thromboses are rarer than was formerly believed. Therefore, vasodilators are definitely indicated for the acute retinal arterial (or arteriolar) occlusion and are best administered by retrobulbar injection. However, the benefits to be derived from a vasodilator as a prophylactic agent are less clear cut. It is most difficult to keep retinal or choroidal vessels dilated. Carbon dioxide inhalation will cause dilatation of choroidal vessels and increased blood flow, but this has not been demonstrated for the more commonly used vasodilators. Nevertheless, it would be wise to use such a drug as nicotinic acid or beta-pyridyl-carbinol tartrate in the management of this patient. The suggested dosage is 50 mg. three times a day.

HEREDITARY TRANSMISSION OF RETINOBLASTOMA

To the Editor:—*A 16-year-old girl had her right eye enucleated at the age of 2 years for a retinoblastoma. The removal of the eye was followed up with x-ray treatments. She has been apparently well since then. At the present time, she is wondering what chances her future children will have of inheriting her eye condition. Genetically speaking, how can one answer her question?*

Abe L. Feuer, M.D., Gastonia, N. C.

Answer.—A great deal of attention has been devoted to this question recently. The data show that only 25% of patients with such sporadic cases transmit the disease to some of their offspring. The reason that 75% of the patients do not have affected offspring is that in some cases the mutation is in the somatic cells only, in some the family size was

too small to permit affected offspring from appearing due to chance factors, or, perhaps, in some a nongenetic accident occurred. If the girl is a transmitter, less than 50% of her children could be expected to have retinoblastoma, since the dominant gene is not always expressed. It is thought that the expectation is about 40% that each child would develop the trait instead of the 50% expectation when the trait is always expressed if the gene for it is present. Tucker and others give a more complete explanation (*A. M. A. Arch. Ophth.* 57:532, 1957).

IPRONIAZID FOR ANGINA PECTORIS

To the Editor:—*The question and answer concerning heart disease and hemoptysis in* The Journal, *March 15, 1958, page 1401, prompted this question on the use of iproniazid in the following case. The patient, 78 years of age, is asymptomatic except for nerve precordial sensations (no real pain) on effort. He is slightly underweight but has never been hypertensive. Findings in the usual laboratory examinations are normal. The electrocardiogram reveals some heart block, and slight enlargement is shown on x-ray. His pulse rate is usually in the low 60's. The history is noncontributory. Would it be advisable to use iproniazid in this case? How and when should it be given, and in what dosage?*

Louis Shalet, M.D., Jamaica, N. Y.

Answer.—Iproniazid should be given only under supervision and by persons who have experience with the drug. It has recently been used in treatment of angina pectoris; reports were first published by Cossio (Buenos Aires) and Cesarman (Mexico City) a year ago and last October respectively. Iproniazid is an unusual drug, very helpful in angina pectoris, but it has to be used with caution because of toxic side-reactions. There will be papers published on this subject, and it is not advisable to use the drug at present, particularly in a 78-year-old man.

TOXICITY OF "TALC"

To the Editor:—*Could soapstone particles ("talc"), if inhaled over a prolonged period of time, produce fibrosis of the lungs?*

Burt Friedman, M.D., Memphis, Tenn.

Answer.—There are many different forms of talc (soapstone or steatite), which basically is a hydrous magnesium silicate. This compound per se is not fibrogenic, but most commercial preparations of talc contain varying amounts of tremolite, which is a fibrous magnesium silicate. Lung fibrosis resembling asbestosis can result from heavy and prolonged exposures to such fibrous compounds, including typical asbestos bodies in the microscopic sections. Also, some talc preparations may have quartz impurities, which might result in a lung fibrosis resembling silicosis after heavy and prolonged exposures. Specimens of the talc under suspicion ought to be given careful minerological studies before too definite conclusions are drawn.

"WHITE VISION"

To the Editor:—*A 45-year-old man has had both eyes removed and now complains of "white vision" present almost continuously while he is awake. He notes that emotional upsets make it worse. His history is somewhat vague. His mother is said to have had rubella before he was born. One eye was removed at the age of 6 months because of a tumor of some sort. He apparently had a congenital cataract on both eyes. In 1935, the cataract was removed and his vision was improved but was still far from normal (he states 40% of normal). In 1942, this remaining eye was removed for intractable pain (glaucoma) and the white vision sensation. He has never been free of this sensation except for a few days at a time since then. Is there any therapy for this condition? Is there any known cause?*

M.D., Ohio.

Answer.—"White vision" is not rare in adults who have had both eyes enucleated. The onset very soon after removal of the second eye and at the age of 26 years, as well as its practically stationary course for 16 years, strongly suggests the manifestation of a psychic trauma in a hypersensitive individual. Had the cause been a cicatrix, neuroma, or other condition of the optic nerve or brain, the white vision would have had other clinical characteristics. There is no specific cure. Treatment involves (1) the practical care of any ocular or other condition which may be aggravative and increase a tendency to become worse as the patient grows older; (2) physical and, especially, mental hygiene; (3) the experimental use of tranquilizing drugs, which may be of temporary value, especially during periods of stress and emotional upset; and (4) psychiatric treatment with or without hypnosis. The latter treatment is not promising, because of the patient's age and the duration of the white vision sensation.

HOSPITALS FOR PATIENTS ADDICTED TO NARCOTICS

To the Editor:—*Please supply names of hospitals where dope addicts go to be cured.*

V. W. Swayze, M.D., Muscatine, Iowa.

Answer.—Persons who are addicted to opiates or the synthetic equivalents of opiates, marihuana, or cocaine are eligible for admission to the U. S. Public Health Service hospitals at Fort Worth, Texas, or Lexington, Ky. Generally, addicts in areas east of the Mississippi are accepted at Lexington, and those west of the Mississippi are treated at Fort Worth. Information and the necessary blanks for requesting admission can be obtained by writing to the medi-

cal officer in charge of either institution. Patients should not go to the hospital until they have been notified that a bed is available. In addition to these federal hospitals, a number of private sanitariums accept addicts, and, in many states, provision for treatment in one of the state mental hospitals can be made. Information must be obtained by writing directly to the sanitarium or to the head of the state hospital system.

PREVENTION OF INGUINAL HERNIA

To the Editor:—*As medical adviser to an aviation corporation, a physician has been confronted with the fact that, although the pilots and mechanics have passed rigid physical examinations before employment, including careful screening for hernia, a great number of them sooner or later develop hernia. It seems that, with proper precautions in regard to lifting and with regular exercises for strengthening the abdominal muscles, this incidence may be definitely reduced. Is there any simple pamphlet of information and instruction along these lines which could be made available to these employees so as to help prevent this situation in the future?*

Paul E. Adolph, M.D., Wheaton, Ill.

Answer.—It is assumed that the inquirer refers to inguinal hernia. This consultant knows of no pamphlet that can be procured with instructions on exercises or precautions for preventing the development of such hernias. Unfortunately, most inguinal hernias developing later in life or those of the direct type result from gradual wearing out of the transversalis fascia. Exercises would be of little value in preventing such hernias, but the avoidance of obesity, as well as attention to any symptoms of urinary obstruction, would aid in reducing their occurrence. A good erect protrusion also is of some help as an aid in protecting this area, as the so-called shutter action on the conjoined tendon.

EFFECT OF DECREASED OXYGEN ON BRAIN CELLS

To the Editor:—*What effect does difficult breathing, causing oxygen lack, and cyanosis have on the brain cells, with special reference to severe, chronic bronchial asthma of many years standing?*

J. M. Hesser, M.D., Benson, Ariz.

Answer.—In patients with chronic asthmatic dyspnea and cyanosis of moderate degree, the brain cells, in all probability, have become acclimatized to oxygen-want and are therefore not damaged. However, in acute, severe asthmatic dyspnea, in which the arterial oxygen saturation declines to very low levels, pathological changes in the brain may take place. The cortex, especially the frontal lobe cortex, is the most oxygen-sensitive organ. With more severe hypoxia, the medulla may be involved, with adverse effect on the respiratory center. The relative sensitivity of various parts of the brain to lack of oxygen was described by Morrison (*Arch. Neurol. & Psychiat.* **55**:1, 1946). The effects of hypoxia due to high altitude, as well as respiratory disease, are reviewed by Barach (Physiologic Therapy in Respiratory Disease, Philadelphia, J. B. Lippincott Company, 1948).

TOXICITY OF NEOMYCIN

To the Editor:—*A patient developed motor paralysis of both legs and loss of sensation in both hands after intramuscular injection of neomycin. 1. Have neurological complications to neomycin been previously reported? 2. Do such complications usually affect more prevalently the central nervous system or the peripheral nervous system? 3. Are the sensory or the motor nerves prevalently affected by these complications? 4. Is a written permit from the patient or his next of kin necessary before injection of neomycin? 5. Is a skin test for allergy necessary in order to avoid the dangers of neurological complications due to neomycin?*

Conrad M. Ayres, M.D., New York.

Answer.—1. The neurological complications due to neomycin have been those which affect the eighth cranial nerve in a way similar to those produced by streptomycin and dihydrostreptomycin. 2. Neither the central nervous system nor the peripheral nervous system is affected except as mentioned above. 3. The sensory and motor nerves are not affected. 4. A written permit is not necessary; however, it would be desirable to explain that neomycin may affect the eighth cranial nerve and may have an effect on the kidneys. 5. An allergy skin test is not necessary.

THYROID MEDICATION AND MYOPIA

To the Editor:—*What results are to be expected in giving thyroid medication to adolescent children for progressive myopia? What long-term effects on thyroid function or other endocrine functions are to be expected from long continued use of exogenous thyroid supplied in this manner?*

M.D., Montana.

Answer.—Thyroid medication has been tried without success in the treatment of progressive myopia in children and young adult persons. Its use for this condition is not recommended. Desiccated thyroid substance given in a physiologic dose of 1 to 2 grains (0.06 to 0.13 Gm.) per day will inhibit the production of thyrotropin by the pituitary gland. It may be that, if suppressive doses of this hormone are given for a sufficiently long time, the thyroid gland will be incapable of functioning normally when use of the medicament is stopped. However, in the vast majority of patients who have been given large doses of thyroid sub-

stance over a good many years, the gland resumes normal function when treatment with the hormone is stopped. Transient hypothyroidism may follow while the thyroid gland is recovering from suppression.

ANEMIA DURING PREGNANCY

To the Editor:—*A 25-year-old woman is due to have her baby in four months. Her hemoglobin level is 9.5 Gm. per 100 cc. She has received the usual dosage of iron (ferrous sulfate) daily for the past two months. Does this low level of hemoglobin justify a blood transfusion? What hemoglobin level warrants a transfusion in a pregnant woman? There is no reason to believe that the low level in this case is due to blood loss, although the only test done has been a stool examination for occult blood. Presumably the cause is nutritional.* *M.D., Connecticut.*

Answer.—A transfusion of whole blood is rarely justified at this stage of pregnancy. A hemoglobin level of less than 10 Gm. per 100 cc. at or near term is the usual criterion for a transfusion. Iron deficiency is the most common cause of anemia during pregnancy. If orally given iron has failed to raise a low hemoglobin level after a two-month period, it is reasonable to assume that the patient is not absorbing or utilizing the iron. A combination of iron and cobalt might prove effective. If there is reason to suspect that the patient has not taken the prescribed medicament, intramuscularly administered iron would solve the problem.

EPILEPSY AND DIPHTHERIA

To the Editor:—*Could epilepsy develop as a result of a diphtheria infection?*

H. Harris, M.D., Hartford, Conn.

Answer.—There are no references available on development of epilepsy as a result of infection by Corynebacterium diphtheriae. If involvement of the nervous system occurs, it usually is a toxic neuritis or polyneuritis with consequent motor paralysis. Convulsive seizures are not a characteristic manifestation of diphtheria.

EXCESSIVE UNDERARM PERSPIRATION

To the Editor:—*Is there any effective treatment for excessive underarm sweating? This situation is most distressing to several teen-aged patients. Anticholinergic drugs, applied locally as creams and given orally, have been tried with little success.* *Norman R. Bates, M.D., Vashon, Wash.*

Answer.—This problem appears to have no satisfactory solution at present. The proprietary antiperspirants are really quite good, on the whole, and a try of a variety of them is worthwhile. A 10% formaldehyde solution in rubbing alcohol might be tolerable and efficacious; however, it irritates some persons, especially blonds, and its odor is objectionable. Some dermatologists (not all) will countenance x-ray therapy in doses of 300 r at about 120 kv. without added filtration at intervals of two weeks until a total dose of 1,800 r may be reached; this consultant does not recommend it. Phenobarbital is to be considered for occasional use.

EROSION OF THE CERVIX

To the Editor:—*If the results of a Schiller's test are chronic ulcerative cervicitis or chronic ulcerative cervicitis with squamous cell metaplasia, what are the therapeutic indications for patients in their forties with such disease? Please give the indications for hysterectomy in these cases.*

M.D., Illinois.

Answer.—Erosion of the cervix, per se, is no indication for hysterectomy in patients in their forties. Tissue examiners in any hospital will question the need for hysterectomy in such cases unless there are other complications, such as fibromyomas, excessive uterine bleeding, endometrial polyps, adenomyosis, endometriosis, or other pathological disorders. Advantage may be taken of Papanicolaou smears for cancer detection as an aid to the other techniques.

COMPOSITION OF EARWAX

To the Editor:—*What is the chemical composition of cerumen (earwax)? What are the best solvents to use in softening this prior to removal or irrigation? Have the common household detergents been applied as possible solvents?*

M.D., Wisconsin.

Answer.—Cerumen is a mixture of the secretory products of the two glands in the cartilaginous portion of the external auditory canal: sebum from the sebaceous gland, and apocrine sweat from the ceruminal gland. Desquamated epithelial cells, dust, and shed hairs are mixed into the cerumen. Tap water, 1 to 2% saline solution, and 1.5 to 3% hydrogen peroxide provide a rapid disintegrating effect on cerumen. In this connection, solutions of some of the common household detergents have been used.

CARCINOMA OF THE BREAST

To the Editor:—*Are there any tests available to determine whether a patient with metastatic and diffuse cancer of the breast will respond favorably to oophorectomy, adrenalectomy, or hypophysectomy?* *M.D., Kentucky.*

Answer.—There are no simple tests available. The details of provocative testing to determine which type of hormone will or will not stimulate a breast cancer are described in the monograph by Jessiman and Moore (Carcinoma of the Breast, Boston, Little, Brown & Company, 1956).